

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification n <sup>6</sup> : C07K 14/47		A2	(11) International Publication Number: WO 99/57144
			(43) International Publication Date: 11 November 1999 (11.11.99)
(21) International Application Number: PCT/US99/09935 (22) International Filing Date: 4 May 1999 (04.05.99) (30) Priority Data: 60/084,254 5 May 1998 (05.05.98) US 60/095,827 7 August 1998 (07.08.98) US 60/102,745 2 October 1998 (02.10.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications US 60/084,254 (CIP) Filed on 5 May 1998 (05.05.98) US 60/095,827 (CIP) Filed on 7 August 1998 (07.08.98) US 60/102,745 (CIP) Filed on 2 October 1998 (02.10.98) (71) Applicant (for all designated States except US): INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View,		CA 94040 (US). BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). REDDY, Roopa [IN/US]; 1233 W. McKinley Drive, Sunnyvale, CA 94086 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). GERSTIN, Edward, H. [US/US]; 1408 38th Avenue, San Francisco, CA 94122 (US). PATTERSON, Chandra [US/US]; 490 Sherwood Way #1, Menlo Park, CA 94025 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). AZIMZAI, Yalda [US/US]; 2045 Rock Springs Drive, Hayward, CA 94547 (US). LU, Dyung, Aina, M. [US/US]; 55 Park Belmont Place, San Jose, CA 95136 (US). (74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published Without international search report and to be republished upon receipt of that report.	

(54) Title: HUMAN TRANSCRIPTIONAL REGULATOR MOLECULES

## (57) Abstract

The invention provides human transcriptional regulator molecules (HTRM) and polynucleotides which identify and encode HTRM. The invention also provides expression vectors, host cells, antibodies, agonists and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of HTRM.

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## HUMAN TRANSCRIPTIONAL REGULATOR MOLECULES

### TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of human transcriptional regulator molecules and to the use of these sequences in the diagnosis, treatment, and prevention of cell proliferative and immune disorders.

### BACKGROUND OF THE INVENTION

Differential control of gene expression is essential to the growth and development of all multicellular organisms. Although gene expression can be controlled at many steps along the path from DNA to protein, the major control point for most genes is at the initiation of transcription. This critical step is regulated both positively and negatively by a combination of general and tissue specific transcription factors, the majority of which function to regulate transcription of one or more target genes.

Mutations in transcription factors (TFs) contribute to oncogenesis. This is probably due to the role of transcription factors on the expression of genes involved in cell proliferation. For example, mutations in transcription factors encoded by proto-oncogenes, such as Fos, Jun, Myc, Rel, and Spi-1, may be oncogenic due to increased stimulation of cell proliferation. Conversely, mutations in transcription factors encoded by tumor suppressor genes, such as p53, RB1, and WT1, may be oncogenic due to decreased inhibition of cell proliferation. (Latchman, D. (1995) Gene Regulation: A Eukaryotic Perspective, Chapman and Hall, London, UK, pp 242-255.)

Many transcription factors are modular proteins that contain separate domains for DNA binding and transcriptional regulation. The DNA binding domain interacts with specific DNA sequences (control elements) near to or within the promoter region of the gene. This interaction brings the regulatory domain of the TF into a position where it can interact with other proteins to stimulate or repress transcription. Many TFs require dimerization or multimerization to be fully functional. Five different types of transcription factors have been described based on five well characterized structural motifs. These five types are the helix-turn-helix, zinc finger, leucine zipper, and helix-loop-helix (HLH) proteins and the steroid-hormone receptors.

The helix-turn-helix motif consists of two  $\alpha$  helices held at a fixed angle. The two helices are connected by a short chain of amino acids, which represents the "turn". The more carboxyl-terminal helix is called the recognition helix and fits into the major groove of the DNA double helix. The recognition helix, whose amino acid side chains differ from protein to protein, plays an

important role in recognizing the specific DNA sequence to which the protein binds. All of the helix-turn-helix proteins bind DNA as dimers in which the two copies of the recognition helix are separated by exactly one turn of the DNA helix. Homeodomain proteins are a special class of helix-turn-helix protein. The homeodomain is folded into three  $\alpha$  helices which are packed tightly together by hydrophobic interactions. Helices two and three closely resemble the helix-turn-helix motif, with the third helix acting as the recognition helix. Proteins containing homeodomain motifs often function as developmental switches.

The zinc finger motif consists of an  $\alpha$  helix and antiparallel  $\beta$  sheet held together by a zinc atom. The zinc finger motif is usually repeated in a tandem array within a protein, such that the  $\alpha$  helix of each zinc finger in the protein makes contact with the major groove of the DNA double helix. This repeated contact between the protein and the DNA produces a strong and specific DNA-protein interaction. The strength and specificity of the interaction can be regulated by the number of zinc finger motifs within the protein.

The leucine zipper motif consists of a single  $\alpha$  helix which is involved in both protein dimerization and DNA binding. Two proteins containing leucine zippers can dimerize by interactions between hydrophobic amino acid residues, commonly leucines, that extend from one side of their respective  $\alpha$  helices. In this way, the  $\alpha$  helices of each protein monomer dimerize to form a short coiled-coil. Just beyond this coiled-coil, the two  $\alpha$  helices separate to form a Y-shaped structure which contacts the major groove of the DNA. Leucine zipper proteins may form homodimers, in which the two protein monomers are identical, or heterodimers, in which the two protein monomers are different. The specificity of DNA binding depends on the dimer formed, since each protein monomer has distinct DNA-binding specificities.

The helix-loop-helix (HLH) motif consists of a short  $\alpha$  helix connected by a loop to a second, longer  $\alpha$  helix. The flexible loop allows the two helices to fold back and pack together. As with the leucine zipper, the HLH motif is involved in both protein dimerization and DNA binding. The dimers can be homodimers or heterodimers, thus increasing the repertoire of DNA-binding sites to which HLH proteins can bind.

The steroid-hormone receptors contain a motif composed of two perpendicular  $\alpha$  helices. In the absence of ligand the steroid-hormone receptors assume a conformation which sequesters the  $\alpha$  helices. Binding of ligand, commonly steroid hormones, thyroid hormones, retinoids, or vitamin D, to the receptor causes a conformational change which exposes the  $\alpha$  helices. The first  $\alpha$  helix contains about seventy residues and includes eight conserved cysteines. This helix fits into the major groove of the DNA double helix and enables DNA-receptor binding. The second  $\alpha$  helix provides for protein dimerization. As with leucine zipper and HLH proteins, both homodimers and heterodimers may be formed by steroid-hormone receptors.



Hundreds of regulatory proteins from a wide variety of organisms have been identified. Most of these proteins have at least one of the common structural motifs described. However, several important regulatory proteins, including the p53 tumor suppressor, have a unique structure not shared with other known regulatory molecules. (Faisst, S. and S. Meyer (1992) Nucl. Acids Res. 20:3-26.) Moreover, other domains of the regulatory proteins often form crucial contacts with the DNA, thereby affecting binding specificity. Accessory proteins can also provide important interactions which may convert a particular regulatory protein from an activator to a repressor, from a repressor to an activator, or it may prevent DNA binding by the regulatory protein completely.

10 The discovery of new human transcriptional regulator molecules and the polynucleotides encoding them satisfies a need in the art by providing new compositions which are useful in the diagnosis, prevention, and treatment of cell proliferative and immune disorders.

### SUMMARY OF THE INVENTION

15 The invention features substantially purified polypeptides, human transcriptional regulator molecules, referred to collectively as "HTRM". In one aspect, the invention provides a substantially purified polypeptide comprising an amino acid sequence selected from the group consisting of

20 SEQ ID NO:1-65, and fragments thereof.

The invention further provides a substantially purified variant having at least 90% amino acid identity to at least one of the amino acid sequences selected from the group consisting of SEQ ID

NO:1-65, and fragments thereof. The invention also provides an isolated and purified polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of

25 SEQ ID NO:1-65, and fragments thereof. The invention also includes an isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting

30 of  
SEQ ID NO:1-65, and fragments thereof.

Additionally, the invention provides an isolated and purified polynucleotide which hybridizes under stringent conditions to the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. The invention also provides an isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide encoding the polypeptide comprising the amino

acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof.

The invention also provides an isolated and purified polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof. The invention further provides an isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof. The invention also provides an isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof.

10 The invention also provides a method for detecting a polynucleotide in a sample containing nucleic acids, the method comprising the steps of (a) hybridizing the complement of the polynucleotide sequence to at least one of the polynucleotides of the sample, thereby forming a hybridization complex; and (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of a polynucleotide in the sample. In one aspect, the method further comprises amplifying the polynucleotide prior to hybridization.

15 The invention further provides an expression vector containing at least a fragment of the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. In another aspect, the expression vector is contained within a host cell.

20 The invention also provides a method for producing a polypeptide, the method comprising the steps of: (a) culturing the host cell containing an expression vector containing at least a fragment of a polynucleotide under conditions suitable for the expression of the polypeptide; and (b) recovering the polypeptide from the host cell culture.

The invention also provides a pharmaceutical composition comprising a substantially purified polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof, in conjunction with a suitable pharmaceutical carrier.

25 The invention further includes a purified antibody which binds to a polypeptide selected from the group consisting of SEQ ID NO:1-65, and fragments thereof. The invention also provides a purified agonist and a purified antagonist to the polypeptide.

30 The invention also provides a method for treating or preventing a disorder of cell proliferation associated with decreased expression or activity of HTRM, the method comprising administering to a subject in need of such treatment an effective amount of a pharmaceutical composition comprising a substantially purified polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof, in conjunction with a suitable pharmaceutical carrier.

The invention also provides a method for treating or preventing a disorder of cell proliferation associated with increased expression or activity of HTRM, the method comprising administering to a subject in need of such treatment an effective amount of an antagonist of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-5 65, and fragments thereof.

### BRIEF DESCRIPTION OF THE TABLES

Table 1 shows nucleotide and polypeptide sequence identification numbers (SEQ ID NO), clone identification numbers (clone ID), cDNA libraries, and cDNA fragments used to assemble 10 full-length sequences encoding HTRM.

Table 2 shows features of each polypeptide sequence including potential motifs, homologous sequences, and methods and algorithms used for identification of HTRM.

Table 3 shows the tissue-specific expression patterns of each nucleic acid sequence as determined by northern analysis, diseases, disorders, or conditions associated with these tissues, 15 and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which Incyte cDNA clones encoding HTRM were isolated.

Table 5 shows the programs, their descriptions, references, and threshold parameters used to analyze HTRM.

20

### DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology used herein is for the 25 purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an 30 antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any machines, materials, and methods similar or equivalent to those described 35 herein can be used to practice or test the present invention, the preferred machines, materials and

methods are now described. All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

## DEFINITIONS

"HTRM" refers to the amino acid sequences of substantially purified HTRM obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and preferably the human species, from any source, whether natural, synthetic, semi-synthetic, or recombinant.

The term "agonist" refers to a molecule which, when bound to HTRM, increases or prolongs the duration of the effect of HTRM. Agonists may include proteins, nucleic acids, carbohydrates, or any other molecules which bind to and modulate the effect of HTRM.

An "allelic variant" is an alternative form of the gene encoding HTRM. Allelic variants may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. Any given natural or recombinant gene may have none, one, or many allelic forms. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

"Altered" nucleic acid sequences encoding HTRM include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polynucleotide the same as HTRM or a polypeptide with at least one functional characteristic of HTRM. Included within this definition are polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding HTRM, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding HTRM. The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent HTRM. Deliberate amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of HTRM is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid, positively charged amino acids may include lysine and arginine, and amino acids with uncharged polar head groups having similar hydrophilicity values may include leucine, isoleucine, and valine; glycine and alanine; asparagine and glutamine; serine and threonine; and

phenylalanine and tyrosine.

The terms "amino acid" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. In this context, "fragments," "immunogenic fragments," or "antigenic fragments" refer to fragments of HTRM which are preferably at least 5 to about 15 amino acids in length, most preferably at least 14 amino acids, and which retain some biological activity or immunological activity of HTRM. Where "amino acid sequence" is recited to refer to an amino acid sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence. Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known in the art.

The term "antagonist" refers to a molecule which, when bound to HTRM, decreases the amount or the duration of the effect of the biological or immunological activity of HTRM. Antagonists may include proteins, nucleic acids, carbohydrates, antibodies, or any other molecules which decrease the effect of HTRM.

The term "antibody" refers to intact molecules as well as to fragments thereof, such as Fab, F(ab')<sub>2</sub>, and Fv fragments, which are capable of binding the epitopic determinant. Antibodies that bind HTRM polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that fragment of a molecule (i.e., an epitope) that makes contact with a particular antibody. When a protein or a fragment of a protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which bind specifically to antigenic determinants (given regions or three-dimensional structures on the protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition containing a nucleic acid sequence which is complementary to the "sense" strand of a specific nucleic acid sequence. Antisense molecules may be produced by any method including synthesis or transcription. Once introduced into a cell, the complementary nucleotides combine with natural sequences produced by the cell to form

duplexes and to block either transcription or translation. The designation "negative" can refer to the antisense strand, and the designation "positive" can refer to the sense strand.

The term "biologically active," refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" refers to the capability of the natural, recombinant, or synthetic HTRM, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence "5' A-G-T 3'" bonds to the complementary sequence "3' T-C-A 5'." Complementarity between two single-stranded molecules may be "partial," such that only some of the nucleic acids bind, or it may be "complete," such that total complementarity exists between the single stranded molecules. The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands. This is of particular importance in amplification reactions, which depend upon binding between nucleic acids strands, and in the design and use of peptide nucleic acid (PNA) molecules.

A "composition comprising a given polynucleotide sequence" or a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or amino acid sequence. The composition may comprise a dry formulation or an aqueous solution. Compositions comprising polynucleotide sequences encoding HTRM or fragments of HTRM may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

"Consensus sequence" refers to a nucleic acid sequence which has been resequenced to resolve uncalled bases, extended using XL-PCR kit (Perkin-Elmer, Norwalk CT) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from the overlapping sequences of more than one Incyte Clone using a computer program for fragment assembly, such as the GELVIEW Fragment Assembly system (GCG, Madison WI). Some sequences have been both extended and assembled to produce the consensus sequence.

The term "correlates with expression of a polynucleotide" indicates that the detection of the presence of nucleic acids, the same or related to a nucleic acid sequence encoding HTRM, by northern analysis is indicative of the presence of nucleic acids encoding HTRM in a sample, and thereby correlates with expression of the transcript from the polynucleotide encoding HTRM.

A "deletion" refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

The term "derivative" refers to the chemical modification of a polypeptide sequence, or a polynucleotide sequence. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

10 The term "similarity" refers to a degree of complementarity. There may be partial similarity or complete similarity. The word "identity" may substitute for the word "similarity." A partially complementary sequence that at least partially inhibits an identical sequence from hybridizing to a target nucleic acid is referred to as "substantially similar." The inhibition of hybridization of the completely complementary sequence to the target sequence may be examined  
15 using a hybridization assay (Southern or northern blot, solution hybridization, and the like) under conditions of reduced stringency. A substantially similar sequence or hybridization probe will compete for and inhibit the binding of a completely similar (identical) sequence to the target sequence under conditions of reduced stringency. This is not to say that conditions of reduced stringency are such that non-specific binding is permitted, as reduced stringency conditions  
20 require that the binding of two sequences to one another be a specific (i.e., a selective) interaction. The absence of non-specific binding may be tested by the use of a second target sequence which lacks even a partial degree of complementarity (e.g., less than about 30% similarity or identity). In the absence of non-specific binding, the substantially similar sequence or probe will not hybridize to the second non-complementary target sequence.

25 The phrases "percent identity" or "% identity" refer to the percentage of sequence similarity found in a comparison of two or more amino acid or nucleic acid sequences. Percent identity can be determined electronically, e.g., by using the MEGALIGN program (DNASTAR, Madison WI) which creates alignments between two or more sequences according to methods selected by the user, e.g., the clustal method. (See, e.g., Higgins, D.G. and P.M. Sharp (1988)  
30 Gene 73:237-244.) The clustal algorithm groups sequences into clusters by examining the distances between all pairs. The clusters are aligned pairwise and then in groups. The percentage similarity between two amino acid sequences, e.g., sequence A and sequence B, is calculated by dividing the length of sequence A, minus the number of gap residues in sequence A, minus the number of gap residues in sequence B, into the sum of the residue matches between sequence A  
35 and sequence B, times one hundred. Gaps of low or of no similarity between the two amino acid

sequences are not included in determining percentage similarity. Percent identity between nucleic acid sequences can also be counted or calculated by other methods known in the art, e.g., the Jotun Hein method. (See, e.g., Hein, J. (1990) *Methods Enzymol.* 183:626-645.) Identity between sequences can also be determined by other methods known in the art, e.g., by varying  
5 hybridization conditions.

"Human artificial chromosomes" (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the elements required for stable mitotic chromosome segregation and maintenance.

The term "humanized antibody" refers to antibody molecules in which the amino acid  
10 sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

"Hybridization" refers to any process by which a strand of nucleic acid binds with a complementary strand through base pairing.

The term "hybridization complex" refers to a complex formed between two nucleic acid  
15 sequences by virtue of the formation of hydrogen bonds between complementary bases. A hybridization complex may be formed in solution (e.g.,  $C_0t$  or  $R_0t$  analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have been fixed).

20 The words "insertion" or "addition" refer to changes in an amino acid or nucleotide sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively, to the sequence found in the naturally occurring molecule.

"Immune response" can refer to conditions associated with inflammation, trauma, immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by  
25 expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

The term "microarray" refers to an arrangement of distinct polynucleotides on a substrate.

The terms "element" or "array element" in a microarray context, refer to hybridizable polynucleotides arranged on the surface of a substrate.

30 The term "modulate" refers to a change in the activity of HTRM. For example, modulation may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of HTRM.

The phrases "nucleic acid" or "nucleic acid sequence" refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or  
35 RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may



represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material. In this context, "fragments" refers to those nucleic acid sequences which, when translated, would produce polypeptides retaining some functional characteristic, e.g., antigenicity, or structural domain characteristic, e.g., ATP-binding site, of the full-length polypeptide.

The terms "operably associated" or "operably linked" refer to functionally related nucleic acid sequences. A promoter is operably associated or operably linked with a coding sequence if the promoter controls the translation of the encoded polypeptide. While operably associated or operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements, e.g., repressor genes, are not contiguously linked to the sequence encoding the polypeptide but still bind to operator sequences that control expression of the polypeptide.

The term "oligonucleotide" refers to a nucleic acid sequence of at least about 6 nucleotides to 60 nucleotides, preferably about 15 to 30 nucleotides, and most preferably about 20 to 25 nucleotides, which can be used in PCR amplification or in a hybridization assay or microarray. "Oligonucleotide" is substantially equivalent to the terms "amplimer," "primer," "oligomer," and "probe," as these terms are commonly defined in the art.

"Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding HTRM, or fragments thereof, or HTRM itself, may comprise a bodily fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

The terms "specific binding" or "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, or an antagonist. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide containing the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

The term "stringent conditions" refers to conditions which permit hybridization between polynucleotides and the claimed polynucleotides. Stringent conditions can be defined by salt concentration, the concentration of organic solvent, e.g., formamide, temperature, and other

conditions well known in the art. In particular, stringency can be increased by reducing the concentration of salt, increasing the concentration of formamide, or raising the hybridization temperature.

The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least about 60% free, preferably about 75% free, and most preferably about 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acids or nucleotides by different amino acids or nucleotides, respectively.

10 "Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

"Transformation" describes a process by which exogenous DNA enters and changes a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type of host cell being transformed and may include, but is not limited to, viral infection, electroporation, heat shock, lipofection, and particle bombardment.

20 The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "variant" of HTRM polypeptides refers to an amino acid sequence that is altered by one or more amino acid residues. The variant may have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties (e.g., replacement of leucine with isoleucine). More rarely, a variant may have "nonconservative" changes (e.g., replacement of glycine with tryptophan). Analogous minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without abolishing biological or immunological activity may be found using computer programs well known in the art, for example, LASERGENE software (DNASTAR).

30

The term "variant," when used in the context of a polynucleotide sequence, may encompass a polynucleotide sequence related to HTRM. This definition may also include, for example, "allelic" (as defined above), "splice," "species," or "polymorphic" variants. A splice variant may have significant identity to a reference molecule, but will generally have a greater or

35

lesser number of polynucleotides due to alternate splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or an absence of domains. Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will have significant amino acid identity relative to each other. A

5 polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a propensity for a disease state.

## 10 THE INVENTION

The invention is based on the discovery of new human transcriptional regulator molecules (HTRM), the polynucleotides encoding HTRM, and the use of these compositions for the diagnosis, treatment, or prevention of cell proliferative and immune disorders.

Table 1 lists the Incyte Clones used to derive full length nucleotide sequences encoding  
15 HTRM. Columns 1 and 2 show the sequence identification numbers (SEQ ID NO) of the amino acid and nucleic acid sequences, respectively. Column 3 shows the Clone ID of the Incyte Clone in which nucleic acids encoding each HTRM were identified, and column 4, the cDNA libraries from which these clones were isolated. Column 5 shows Incyte clones, their corresponding cDNA libraries, and shotgun sequences. The clones and shotgun sequences are part of the consensus  
20 nucleotide sequence of each HTRM and are useful as fragments in hybridization technologies.

The columns of Table 2 show various properties of the polypeptides of the invention: column 1 references the SEQ ID NO; column 2 shows the number of amino acid residues in each polypeptide; column 3, potential phosphorylation sites; column 4, potential glycosylation sites; column 5, the amino acid residues comprising signature sequences and motifs; column 6, the  
25 identity of each protein; and column 7, analytical methods used to identify each protein through sequence homology and protein motifs.

The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions associated with nucleotide sequences encoding HTRM. The first column of Table 3 lists the nucleotide sequence identifiers. The second column lists tissue categories which express HTRM as  
30 a fraction of total tissue categories expressing HTRM. The third column lists the diseases, disorders, or conditions associated with those tissues expressing HTRM. The fourth column lists the vectors used to subclone the cDNA library.

The following fragments of the nucleotide sequences encoding HTRM are useful in hybridization or amplification technologies to identify SEQ ID NO:110-130 and to distinguish  
35 between SEQ ID NO:110-130 and related polynucleotide sequences. The useful fragments are the

fragment of SEQ ID NO:110 from about nucleotide 273 to about nucleotide 317; the fragment of SEQ ID NO:111 from about nucleotide 217 to about nucleotide 261 the fragment of SEQ ID NO:112 from about nucleotide 273 to about nucleotide 308; the fragment of SEQ ID NO:113 from about nucleotide 163 to about nucleotide 207; the fragment of SEQ ID NO:114 from about  
5 nucleotide 433 to about nucleotide 477; the fragment of SEQ ID NO:115 from about nucleotide 597 to about nucleotide 641; the fragment of SEQ ID NO:116 from about nucleotide 111 to about nucleotide 146; the fragment of SEQ ID NO:117 from about nucleotide 217 to about nucleotide 261; the fragment of SEQ ID NO:118 from about nucleotide 867 to about nucleotide 911; the fragment of SEQ ID NO:119 from about nucleotide 1082 to about nucleotide 1126; the fragment  
10 of SEQ ID NO:120 from about nucleotide 702 to about nucleotide 748; the fragment of SEQ ID NO:121 from about nucleotide 380 to about nucleotide 424; the fragment of SEQ ID NO:122 from about nucleotide 352 to about nucleotide 396; the fragment of SEQ ID NO:123 from about nucleotide 219 to about nucleotide 263; the fragment of SEQ ID NO:124 from about nucleotide 326 to about nucleotide 370; the fragment of SEQ ID NO:125 from about nucleotide 595 to about  
15 nucleotide 639; the fragment of SEQ ID NO:126 from about nucleotide 272 to about nucleotide 316; the fragment of SEQ ID NO:127 from about nucleotide 163 to about nucleotide 207; the fragment of SEQ ID NO:128 from about nucleotide 271 to about nucleotide 315; the fragment of SEQ ID NO:129 from about nucleotide 866 to about nucleotide 910; and the fragment of SEQ ID NO:130 from about nucleotide 487 to about nucleotide 531.

20 The invention also encompasses HTRM variants. A preferred HTRM variant is one which has at least about 80%, more preferably at least about 90%, and most preferably at least about 95% amino acid sequence identity to the HTRM amino acid sequence, and which contains at least one functional or structural characteristic of HTRM.

The invention also encompasses polynucleotides which encode HTRM. In a particular  
25 embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:66-130, which encodes HTRM.

The invention also encompasses a variant of a polynucleotide sequence encoding HTRM. In particular, such a variant polynucleotide sequence will have at least about 70%, more preferably at least about 85%, and most preferably at least about 95% polynucleotide sequence identity to the  
30 polynucleotide sequence encoding HTRM. A particular aspect of the invention encompasses a variant of a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:66-130 which has at least about 70%, more preferably at least about 85%, and most preferably at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the  
35 group consisting of SEQ ID NO:66-130. Any one of the polynucleotide variants described above

can encode an amino acid sequence which contains at least one functional or structural characteristic of HTRM.

It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding HTRM, some bearing minimal  
5 similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring HTRM, and all such variations are to be  
10 considered as being specifically disclosed.

Although nucleotide sequences which encode HTRM and its variants are preferably capable of hybridizing to the nucleotide sequence of the naturally occurring HTRM under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding HTRM or its derivatives possessing a substantially different codon usage,  
15 e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding HTRM and its derivatives without altering the encoded amino acid sequences include the production of RNA transcripts having more  
20 desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode HTRM and HTRM derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic sequence may be inserted into any of the many available expression vectors and cell  
25 systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a sequence encoding HTRM or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:66-130 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M.  
30 and S.L. Berger (1987) *Methods Enzymol.* 152:399-407; Kimmel, A.R. (1987) *Methods Enzymol.* 152:507-511.) For example, stringent salt concentration will ordinarily be less than about 750 mM NaCl and 75 mM trisodium citrate, preferably less than about 500 mM NaCl and 50 mM trisodium citrate, and most preferably less than about 250 mM NaCl and 25 mM trisodium citrate. Low stringency hybridization can be obtained in the absence of organic solvent, e.g., formamide, while  
35 high stringency hybridization can be obtained in the presence of at least about 35% formamide.

and most preferably at least about 50% formamide. Stringent temperature conditions will ordinarily include temperatures of at least about 30°C, more preferably of at least about 37°C, and most preferably of at least about 42°C. Varying additional parameters, such as hybridization time, the concentration of detergent, e.g., sodium dodecyl sulfate (SDS), and the inclusion or exclusion of carrier DNA, are well known to those skilled in the art. Various levels of stringency are accomplished by combining these various conditions as needed. In a preferred embodiment, hybridization will occur at 30°C in 750 mM NaCl, 75 mM trisodium citrate, and 1% SDS. In a more preferred embodiment, hybridization will occur at 37°C in 500 mM NaCl, 50 mM trisodium citrate, 1% SDS, 35% formamide, and 100 µg/ml denatured salmon sperm DNA (ssDNA). In a most preferred embodiment, hybridization will occur at 42°C in 250 mM NaCl, 25 mM trisodium citrate, 1% SDS, 50 % formamide, and 200 µg/ml ssDNA. Useful variations on these conditions will be readily apparent to those skilled in the art.

The washing steps which follow hybridization can also vary in stringency. Wash stringency conditions can be defined by salt concentration and by temperature. As above, wash stringency can be increased by decreasing salt concentration or by increasing temperature. For example, stringent salt concentration for the wash steps will preferably be less than about 30 mM NaCl and 3 mM trisodium citrate, and most preferably less than about 15 mM NaCl and 1.5 mM trisodium citrate. Stringent temperature conditions for the wash steps will ordinarily include temperature of at least about 25°C, more preferably of at least about 42°C, and most preferably of at least about 68°C. In a preferred embodiment, wash steps will occur at 25°C in 30 mM NaCl, 3 mM trisodium citrate, and 0.1% SDS. In a more preferred embodiment, wash steps will occur at 42°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. In a most preferred embodiment, wash steps will occur at 68°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. Additional variations on these conditions will be readily apparent to those skilled in the art.

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (Perkin-Elmer), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the Hamilton MICROLAB 2200 (Hamilton, Reno NV), Peltier Thermal Cycler 200 (PTC200; MJ Research, Watertown MA) and the ABI CATALYST 800 (Perkin-Elmer). Sequencing is then carried out using either ABI 373 or 377 DNA sequencing systems (Perkin-Elmer) or the MEGABACE 1000 DNA sequencing system (Molecular Dynamics, Sunnyvale CA). The resulting sequences are analyzed using a variety of

algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding HTRM may be extended utilizing a partial  
5 nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed, restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) *PCR Methods Applic.* 2:318-322.) Another method, inverse PCR, uses primers that extend in divergent  
10 directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) *Nucleic Acids Res.* 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome DNA. (See, e.g., Lagerstrom, M. et al. (1991) *PCR Methods Applic.* 1:111-119.) In  
15 this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are known in the art. (See, e.g., Parker, J.D. et al. (1991) *Nucleic Acids Res.* 19:3055-306). Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic  
20 DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, Plymouth MN) or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.

25 When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

30 Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal  
35 using appropriate software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, Perkin-Elmer),

and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be present in limited amounts in a particular sample.

In another embodiment of the invention, polynucleotide sequences or fragments thereof which encode HTRM may be cloned in recombinant DNA molecules that direct expression of HTRM, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be produced and used to express HTRM.

The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter HTRM-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

In another embodiment, sequences encoding HTRM may be synthesized, in whole or in part, using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) Nucl. Acids Res. Symp. Ser. 215-223, and Horn, T. et al. (1980) Nucl. Acids Res. Symp. Ser. 225-232.) Alternatively, HTRM itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solid-phase techniques. (See, e.g., Roberge, J.Y. et al. (1995) Science 269:202-204.) Automated synthesis may be achieved using the ABI 431A Peptide Synthesizer (Perkin-Elmer). Additionally, the amino acid sequence of HTRM, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

The peptide may be substantially purified by preparative high performance liquid chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) Methods Enzymol. 182:392-421.) The composition of the synthetic peptides may be confirmed by amino acid analysis or by sequencing. (See, e.g., Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY.)

In order to express a biologically active HTRM, the nucleotide sequences encoding HTRM or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as



enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences encoding HTRM. Such elements may vary in their strength and specificity. Specific initiation signals may also be used to achieve more efficient translation of sequences encoding HTRM. Such signals include the ATG initiation codon and adjacent  
5 sequences, e.g. the Kozak sequence. In cases where sequences encoding HTRM and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous  
10 translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct  
15 expression vectors containing sequences encoding HTRM and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. (See, e.g., Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995) Current Protocols in Molecular Biology, John Wiley & Sons,  
20 New York NY, ch. 9, 13, and 16.)

A variety of expression vector/host systems may be utilized to contain and express sequences encoding HTRM. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral  
25 expression vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems. The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected  
30 depending upon the use intended for polynucleotide sequences encoding HTRM. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding HTRM can be achieved using a multifunctional E. coli vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or pSPORT1 plasmid (Life Technologies). Ligation of sequences encoding HTRM into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure  
35 for identification of transformed bacteria containing recombinant molecules. In addition, these

vectors may be useful for in vitro transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509.) When large quantities of HTRM are needed, e.g. for the production of antibodies, vectors which direct high level expression of HTRM  
5 may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of HTRM. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH, may be used in the yeast Saccharomyces cerevisiae or Pichia pastoris. In addition, such vectors  
10 direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, supra; Grant et al. (1987) Methods Enzymol. 153:516-54; and Scorer, C. A. et al. (1994) Bio/Technology 12:181-184.)

Plant systems may also be used for expression of HTRM. Transcription of sequences  
15 encoding HTRM may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used. (See, e.g., Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; and Winter, J. et al. (1991) Results Probl. Cell  
20 Differ. 17:85-105.) These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, sequences encoding HTRM may be ligated  
25 into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses HTRM in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.  
30 SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat Genet.  
35 15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of HTRM in cell lines is preferred. For example, sequences encoding HTRM can be transformed into cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate  
5 vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

10 Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk* or *ap<sup>r</sup>* cells, respectively. (See, e.g., Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers  
15 resistance to methotrexate; *neo* confers resistance to the aminoglycosides, neomycin and G-418; and *als* or *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g., Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., *trpB* and *hisD*, which alter cellular requirements for metabolites. (See, e.g.,  
20 Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech),  $\beta$  glucuronidase and its substrate  $\beta$ -glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) Methods Mol.  
25 Biol. 55:121-131.)

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding HTRM is inserted within a marker gene sequence, transformed cells containing sequences encoding HTRM can be identified by the absence of marker gene  
30 function. Alternatively, a marker gene can be placed in tandem with a sequence encoding HTRM under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

In general, host cells that contain the nucleic acid sequence encoding HTRM and that express HTRM may be identified by a variety of procedures known to those of skill in the art.

35 These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR

amplification, and protein bioassay or immunoassay techniques which include membrane solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein sequences.

Immunological methods for detecting and measuring the expression of HTRM using either  
5 specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on HTRM is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art.  
10 (See, e.g., Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St Paul MN. Sect. IV; Coligan, J. E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press. Totowa NJ).

A wide variety of labels and conjugation techniques are known by those skilled in the art  
15 and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding HTRM include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, the sequences encoding HTRM, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are  
20 commercially available, and may be used to synthesize RNA probes *in vitro* by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia Biotech, Promega (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes,  
25 fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding HTRM may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the  
30 sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode HTRM may be designed to contain signal sequences which direct secretion of HTRM through a prokaryotic or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications  
35 of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation.

phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to specify protein targeting, folding, and/or activity.

Different host cells which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and WI38), are available from the American Type Culture Collection (ATCC, Bethesda MD) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding HTRM may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric HTRM protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of HTRM activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the HTRM encoding sequence and the heterologous protein sequence, so that HTRM may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

In a further embodiment of the invention, synthesis of radiolabeled HTRM may be achieved in vitro using the TNT rabbit reticulocyte lysate or wheat germ extract systems (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, preferably <sup>35</sup>S-methionine.

Fragments of HTRM may be produced not only by recombinant production, but also by direct peptide synthesis using solid-phase techniques. (See, e.g., Creighton, supra, pp. 55-60.) Protein synthesis may be performed by manual techniques or by automation. Automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin-Elmer). Various fragments of HTRM may be synthesized separately and then combined to produce the full length molecule.

## THERAPEUTICS

Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of HTRM and human transcriptional regulator molecules. In addition, the expression of HTRM is closely associated with cell proliferation, inflammation, and the immune response. Therefore, HTRM appears to play a role in cell proliferative and immune disorders. In the treatment of disorders associated with increased HTRM expression or activity, it is desirable to decrease the expression or activity of HTRM. In the treatment of disorders associated with decreased HTRM expression or activity, it is desirable to increase the expression or activity of HTRM.

Therefore, in one embodiment, HTRM or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia; cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; and an immune disorder such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma

In another embodiment, a vector capable of expressing HTRM or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM including, but not limited to, those described above.

In a further embodiment, a pharmaceutical composition comprising a substantially purified HTRM in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM including, but not limited to, those provided above.

5 In still another embodiment, an agonist which modulates the activity of HTRM may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HTRM including, but not limited to, those listed above.

In a further embodiment, an antagonist of HTRM may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of HTRM. Examples of  
10 such disorders include, but are not limited to, those described above. In one aspect, an antibody which specifically binds HTRM may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissue which express HTRM.

In an additional embodiment, a vector expressing the complement of the polynucleotide  
15 encoding HTRM may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of HTRM including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination  
20 therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

25 An antagonist of HTRM may be produced using methods which are generally known in the art. In particular, purified HTRM may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind HTRM. Antibodies to HTRM may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments,  
30 and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are especially preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with HTRM or with any fragment or oligopeptide thereof which has immunogenic properties. Depending on the host species, various  
35 adjuvants may be used to increase immunological response. Such adjuvants include, but are not

limited to. Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

5           It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to HTRM have an amino acid sequence consisting of at least about 5 amino acids, and, more preferably, of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein and contain the entire amino acid sequence of a small, naturally occurring molecule. Short stretches of  
10 HTRM amino acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule may be produced.

Monoclonal antibodies to HTRM may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-  
15 hybridoma technique. (See, e.g., Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. Immunol. Methods 81:31-42; Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. 80:2026-2030; and Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate  
20 antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce HTRM-specific single chain antibodies. Antibodies with related specificity, but of distinct  
25 idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton D.R. (1991) Proc. Natl. Acad. Sci. 88:10134-10137.)

Antibodies may also be produced by inducing in vivo production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. 86:  
30 3833-3837; Winter, G. et al. (1991) Nature 349:293-299.)

Antibody fragments which contain specific binding sites for HTRM may also be generated. For example, such fragments include, but are not limited to, F(ab')<sub>2</sub> fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragments. Alternatively, Fab expression libraries may be  
35 constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired



specificity. (See, e.g., Huse, W.D. et al. (1989) Science 246:1275-1281.)

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between HTRM and its specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering HTRM epitopes is preferred, but a competitive binding assay may also be employed (Pound, supra).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for HTRM. Affinity is expressed as an association constant,  $K_a$ , which is defined as the molar concentration of HTRM-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The  $K_a$  determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple HTRM epitopes, represents the average affinity, or avidity, of the antibodies for HTRM. The  $K_a$  determined for a preparation of monoclonal antibodies, which are monospecific for a particular HTRM epitope, represents a true measure of affinity. High-affinity antibody preparations with  $K_a$  ranging from about  $10^9$  to  $10^{12}$  L/mole are preferred for use in immunoassays in which the HTRM-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with  $K_a$  ranging from about  $10^6$  to  $10^7$  L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of HTRM, preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical Approach, IRL Press, Washington, DC; Liddell, J. E. and Cryer, A. (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is preferred for use in procedures requiring precipitation of HTRM-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al. supra.)

In another embodiment of the invention, the polynucleotides encoding HTRM, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, the complement of the polynucleotide encoding HTRM may be used in situations in which it would be desirable to block the transcription of the mRNA. In particular, cells may be transformed with sequences complementary to polynucleotides encoding HTRM. Thus, complementary molecules

or fragments may be used to modulate HTRM activity, or to achieve regulation of gene function. Such technology is now well known in the art, and sense or antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding HTRM.

5        Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of nucleotide sequences to the targeted organ, tissue, or cell population. Methods which are well known to those skilled in the art can be used to construct vectors to express nucleic acid sequences complementary to the polynucleotides encoding HTRM. (See, e.g., Sambrook, supra; Ausubel, 1995, supra.)

10        Genes encoding HTRM can be turned off by transforming a cell or tissue with expression vectors which express high levels of a polynucleotide, or fragment thereof, encoding HTRM. Such constructs may be used to introduce untranslatable sense or antisense sequences into a cell. Even in the absence of integration into the DNA, such vectors may continue to transcribe RNA molecules until they are disabled by endogenous nucleases. Transient expression may last for a  
15       month or more with a non-replicating vector, and may last even longer if appropriate replication elements are part of the vector system.

As mentioned above, modifications of gene expression can be obtained by designing complementary sequences or antisense molecules (DNA, RNA, or PNA) to the control, 5', or regulatory regions of the gene encoding HTRM. Oligonucleotides derived from the transcription  
20       initiation site, e.g., between about positions -10 and +10 from the start site, are preferred. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee, J.E. et al.  
25       (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the  
30       ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of sequences encoding HTRM.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences:  
35       GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20

ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

5 Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding HTRM. Such DNA sequences may be  
10 incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'  
15 ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by  
20 endogenous endonucleases.

Many methods for introducing vectors into cells or tissues are available and equally suitable for use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers  
25 may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nature Biotechnology 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as dogs, cats, cows, horses, rabbits, monkeys, and most preferably, humans.

30 An additional embodiment of the invention relates to the administration of a pharmaceutical or sterile composition, in conjunction with a pharmaceutically acceptable carrier, for any of the therapeutic effects discussed above. Such pharmaceutical compositions may consist of HTRM, antibodies to HTRM, and mimetics, agonists, antagonists, or inhibitors of HTRM. The compositions may be administered alone or in combination with at least one other agent, such as a  
35 stabilizing compound, which may be administered in any sterile, biocompatible pharmaceutical

carrier including, but not limited to, saline, buffered saline, dextrose, and water. The compositions may be administered to a patient alone, or in combination with other agents, drugs, or hormones.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, 5 intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically-acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used 10 pharmaceutically. Further details on techniques for formulation and administration may be found in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA).

Pharmaceutical compositions for oral administration can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, 15 pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Pharmaceutical preparations for oral use can be obtained through combining active compounds with solid excipient and processing the resultant mixture of granules (optionally, after grinding) to obtain tablets or dragee cores. Suitable auxiliaries can be added, if desired. Suitable 20 excipients include carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, and sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethyl-cellulose, or sodium carboxymethylcellulose; gums, including arabic and tragacanth; and proteins, such as gelatin and collagen. If desired, disintegrating or solubilizing agents may be added, such as the cross-linked polyvinyl pyrrolidone, 25 agar, and alginic acid or a salt thereof, such as sodium alginate.

Dragee cores may be used in conjunction with suitable coatings, such as concentrated sugar solutions, which may also contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for 30 product identification or to characterize the quantity of active compound, i.e., dosage.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with fillers or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft 35 capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty

oils, liquid, or liquid polyethylene glycol with or without stabilizers.

Pharmaceutical formulations suitable for parenteral administration may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. Aqueous injection suspensions may contain  
5 substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils, such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate, triglycerides, or liposomes. Non-lipid polycationic amino polymers may also be used for delivery. Optionally, the  
10 suspension may also contain suitable stabilizers or agents to increase the solubility of the compounds and allow for the preparation of highly concentrated solutions.

For topical or nasal administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

The pharmaceutical compositions of the present invention may be manufactured in a  
15 manner that is known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes.

The pharmaceutical composition may be provided as a salt and can be formed with many acids, including but not limited to, hydrochloric, sulfuric, acetic, lactic, tartaric, malic, and succinic acid. Salts tend to be more soluble in aqueous or other protonic solvents than are the  
20 corresponding free base forms. In other cases, the preferred preparation may be a lyophilized powder which may contain any or all of the following: 1 mM to 50 mM histidine, 0.1% to 2% sucrose, and 2% to 7% mannitol, at a pH range of 4.5 to 5.5, that is combined with buffer prior to use.

After pharmaceutical compositions have been prepared, they can be placed in an  
25 appropriate container and labeled for treatment of an indicated condition. For administration of HTRM, such labeling would include amount, frequency, and method of administration.

Pharmaceutical compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the  
30 art.

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells or in animal models such as mice, rats, rabbits, dogs, or pigs. An animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes  
35 for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example HTRM or fragments thereof, antibodies of HTRM, and agonists, antagonists or inhibitors of HTRM, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the  $ED_{50}$  (the dose therapeutically effective in 50% of the population) or  $LD_{50}$  (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, and it can be expressed as the  $LD_{50}/ED_{50}$  ratio. Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the  $ED_{50}$  with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about  $0.1 \mu\text{g}$  to  $100,000 \mu\text{g}$ , up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

## DIAGNOSTICS

In another embodiment, antibodies which specifically bind HTRM may be used for the diagnosis of disorders characterized by expression of HTRM, or in assays to monitor patients being treated with HTRM or agonists, antagonists, or inhibitors of HTRM. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for HTRM include methods which utilize the antibody and a label to detect HTRM in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known

in the art and may be used.

A variety of protocols for measuring HTRM, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of HTRM expression. Normal or standard values for HTRM expression are established by combining body fluids or cell extracts taken from normal mammalian subjects, preferably human, with antibody to HTRM under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, preferably by photometric means. Quantities of HTRM expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding HTRM may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantitate gene expression in biopsied tissues in which expression of HTRM may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of HTRM, and to monitor regulation of HTRM levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotide sequences, including genomic sequences, encoding HTRM or closely related molecules may be used to identify nucleic acid sequences which encode HTRM. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification (maximal, high, intermediate, or low), will determine whether the probe identifies only naturally occurring sequences encoding HTRM, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and should preferably have at least 50% sequence identity to any of the HTRM encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:66-130 or from genomic sequences including promoters, enhancers, and introns of the HTRM gene.

Means for producing specific hybridization probes for DNAs encoding HTRM include the cloning of polynucleotide sequences encoding HTRM or HTRM derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as  $^{32}\text{P}$  or  $^{35}\text{S}$ , or by enzymatic labels,

such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding HTRM may be used for the diagnosis of disorders associated with expression of HTRM. Examples of such disorders include, but are not limited to, a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia; cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; and an immune disorder such as acquired immunodeficiency syndrome (AIDS). Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma. The polynucleotide sequences encoding HTRM may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered HTRM expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding HTRM may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding HTRM may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantitated and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of nucleotide sequences encoding HTRM in the sample indicates the presence of the associated disorder. Such



assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of HTRM, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding HTRM, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated, hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

Additional diagnostic uses for oligonucleotides designed from the sequences encoding HTRM may involve the use of PCR. These oligomers may be chemically synthesized, generated enzymatically, or produced in vitro. Oligomers will preferably contain a fragment of a polynucleotide encoding HTRM, or a fragment of a polynucleotide complementary to the polynucleotide encoding HTRM, and will be employed under optimized conditions for identification of a specific gene or condition. Oligomers may also be employed under less stringent conditions for detection or quantitation of closely related DNA or RNA sequences.

Methods which may also be used to quantitate the expression of HTRM include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) J. Immunol. Methods 159:235-244; Duplaa, C. et al. (1993) Anal. Biochem. 229-236.) The speed of quantitation of multiple samples may be accelerated by running the assay in an ELISA format where the oligomer of interest is presented in various dilutions and a spectrophotometric or

colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the polynucleotide sequences described herein may be used as targets in a microarray. The microarray can be used to monitor the expression level of large numbers of genes simultaneously  
5 and to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, and to develop and monitor the activities of therapeutic agents.

Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g., Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl.  
10 Acad. Sci. 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.)

In another embodiment of the invention, nucleic acid sequences encoding HTRM may be used to generate hybridization probes useful in mapping the naturally occurring genomic  
15 sequence. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries. (See, e.g., Harrington, J.J. et al. (1997) Nat Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends  
20 Genet. 7:149-154.)

Fluorescent in situ hybridization (FISH) may be correlated with other physical chromosome mapping techniques and genetic map data. (See, e.g., Heinz-Ulrich, et al. (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map data can be found in various scientific  
25 journals or at the Online Mendelian Inheritance in Man (OMIM) site. Correlation between the location of the gene encoding HTRM on a physical chromosomal map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder. The nucleotide sequences of the invention may be used to detect differences in gene sequences among normal, carrier, and affected individuals.

In situ hybridization of chromosomal preparations and physical mapping techniques, such  
30 as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the number or arm of a particular human chromosome is not known. New sequences can be assigned to chromosomal arms by physical mapping. This provides valuable information to investigators searching for disease genes using  
35 positional cloning or other gene discovery techniques. Once the disease or syndrome has been

crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23. any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the subject invention may also be used to detect differences in the chromosomal  
5 location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

In another embodiment of the invention, HTRM, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of  
10 binding complexes between HTRM and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen, et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with HTRM, or  
15 fragments thereof, and washed. Bound HTRM is then detected by methods well known in the art. Purified HTRM can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which  
20 neutralizing antibodies capable of binding HTRM specifically compete with a test compound for binding HTRM. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with HTRM.

In additional embodiments, the nucleotide sequences which encode HTRM may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely  
25 on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of  
30 the remainder of the disclosure in any way whatsoever.

The entire disclosure of all applications, patents, and publications, cited above and below, and of US provisional applications 60/084,254 (filed May 5, 1998), 60/095,827 (filed August 7, 1998), and 60/102,745 (filed Oct. 2, 1998) are hereby incorporated by reference.

## EXAMPLES

### 35 I. Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic solution of phenol and guanidine isothiocyanate. The resulting  
5 lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA purity. In some cases, RNA was treated with DNase. For most libraries, poly(A<sup>+</sup>) RNA was  
10 isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Valencia CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding  
15 cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP vector system (Stratagene) or SUPERScript plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, supra, units 5.1-6.6). Reverse transcription was initiated using oligo d(T) or random primers. Synthetic oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA  
20 was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g., PBLUESCRIPT plasmid (Stratagene), pSPORT1 plasmid  
25 (Life Technologies), or pINCY (Incyte Pharmaceuticals, Palo Alto CA). Recombinant plasmids were transformed into competent *E. coli* cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5 $\alpha$ , DH10B, or ElectroMAX DH10B from Life Technologies.

## II. Isolation of cDNA Clones

Plasmids were recovered from host cells by in vivo excision, using the UNIZAP vector  
30 system (Stratagene) or cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the REAL Prep 96 plasmid kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water  
35 and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-well plates, and the concentration of amplified plasmid DNA was quantified  
5 fluorometrically using PICOGREEN dye (Molecular Probes, Eugene OR) and a Fluoroskan II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

### III. Sequencing and Analysis

The cDNAs were prepared for sequencing using the ABI CATALYST 800 (Perkin-Elmer) or the HYDRA microdispenser (Robbins Scientific) or MICROLAB 2200 (Hamilton) systems in  
10 combination with the PTC-200 thermal cyclers (MJ Research). The cDNAs were sequenced using the ABI PRISM 373 or 377 sequencing systems (Perkin-Elmer) and standard ABI protocols, base calling software, and kits. In one alternative, cDNAs were sequenced using the MEGABACE 1000 DNA sequencing system (Molecular Dynamics). In another alternative, the cDNAs were amplified and sequenced using the ABI PRISM BIGDYE Terminator cycle sequencing ready  
15 reaction kit (Perkin-Elmer). In yet another alternative, cDNAs were sequenced using solutions and dyes from Amersham Pharmacia Biotech. Reading frames for the ESTs were determined using standard methods (reviewed in Ausubel, 1997, supra, unit 7.7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example V.

The polynucleotide sequences derived from cDNA, extension, and shotgun sequencing  
20 were assembled and analyzed using a combination of software programs which utilize algorithms well known to those skilled in the art. Table 5 summarizes the software programs, descriptions, references, and threshold parameters used. The first column of Table 5 shows the tools, programs, and algorithms used, the second column provides a brief description thereof, the third column presents the references which are incorporated by reference herein, and the fourth column  
25 presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the probability the greater the homology). Sequences were analyzed using MACDNASIS PRO software (Hitachi Software Engineering, S. San Francisco CA) and LASERGENE software (DNASTAR).

cDNAs were also compared to sequences in GenBank using a search algorithm developed  
30 by Applied Biosystems and incorporated into the INHERIT™ 670 sequence analysis system. In this algorithm, Pattern Specification Language (TRW Inc, Los Angeles, CA) was used to determine regions of homology. The three parameters that determine how the sequence comparisons run were window size, window offset, and error tolerance. Using a combination of these three parameters, the DNA database was searched for sequences containing regions of  
35 homology to the query sequence, and the appropriate sequences were scored with an initial value.

Subsequently, these homologous regions were examined using dot matrix homology plots to distinguish regions of homology from chance matches. Smith-Waterman alignments were used to display the results of the homology search.

Peptide and protein sequence homologies were ascertained using the INHERIT- 670  
5 sequence analysis system using the methods similar to those used in DNA sequence homologies. Pattern Specification Language and parameter windows were used to search protein databases for sequences containing regions of homology which were scored with an initial value. Dot-matrix homology plots were examined to distinguish regions of significant homology from chance matches.

10 The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programming, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS to acquire annotation, using programs based on  
15 BLAST, FASTA, and BLIMPS. The sequences were assembled into full length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against  
20 databases such as the GenBank databases (described above), SwissProt, BLOCKS, PRINTS, PFAM, and Prosite.

The programs described above for the assembly and analysis of full length polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:110-130. Fragments from about 20 to about 4000 nucleotides which are useful in  
25 hybridization and amplification technologies were described in The Invention section above.

#### IV. Northern Analysis

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7;  
30 Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical or related molecules in nucleotide databases such as GenBank or LIFESEQ database (Incyte Pharmaceuticals). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any  
35 particular match is categorized as exact or similar. The basis of the search is the product score,

which is defined as:

$$\frac{\% \text{ sequence identity} \times \% \text{ maximum BLAST score}}{100}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. For example, with a product score of 40, the match will be exact within a 1% to 2% error, and, with a product score of 70, the match will be exact. Similar molecules are usually identified by selecting those which show product scores between 15 and 40, although lower scores may identify related molecules.

The results of northern analyses are reported a percentage distribution of libraries in which the transcript encoding HTRM occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal, hematopoietic/immune, musculoskeletal, nervous, reproductive, and urologic. The disease categories included cancer, inflammation/trauma, fetal, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories. Percentage values of tissue-specific and disease expression are reported in Table 3.

#### V. Extension of HTRM Encoding Polynucleotides

The full length nucleic acid sequence of SEQ ID NO:66-130 was produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer, to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing  $Mg^{2+}$ ,  $(NH_4)_2SO_4$ , and  $\beta$ -mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme (Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+

were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

The concentration of DNA in each well was determined by dispensing 100 µl PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5 µl of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the concentration of DNA. A 5 µl to 10 µl aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose mini-gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, digested with CviJI cholera virus endonuclease (Molecular Biology Research, Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into competent *E. coli* cells. Transformed cells were selected on antibiotic-containing media, individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% dimethylsulphoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Perkin-Elmer).

In like manner, the nucleotide sequence of SEQ ID NO:66-130 is used to obtain 5' regulatory sequences using the procedure above, oligonucleotides designed for such extension, and an appropriate genomic library.

## VI. Labeling and Use of Individual Hybridization Probes

Hybridization probes derived from SEQ ID NO:66-130 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20



base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250  $\mu$ Ci of [ $\gamma$ - $^{32}$ P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot containing  $10^7$  counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under increasingly stringent conditions up to 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. After XOMAT-AR film (Eastman Kodak, Rochester NY) is exposed to the blots to film for several hours, hybridization patterns are compared visually.

## VII. Microarrays

A chemical coupling procedure and an ink jet device can be used to synthesize array elements on the surface of a substrate. (See, e.g., Baldeschweiler, supra.) An array analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced by hand or using available methods and machines and contain any appropriate number of elements. After hybridization, nonhybridized probes are removed and a scanner used to determine the levels and patterns of fluorescence. The degree of complementarity and the relative abundance of each probe which hybridizes to an element on the microarray may be assessed through analysis of the scanned images.

Full-length cDNAs, Expressed Sequence Tags (ESTs), or fragments thereof may comprise the elements of the microarray. Fragments suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). Full-length cDNAs, ESTs, or fragments thereof corresponding to one of the nucleotide sequences of the present invention, or selected at random from a cDNA library relevant to the present invention, are arranged on an appropriate substrate, e.g., a glass slide. The cDNA is fixed to the slide using, e.g., UV cross-linking followed by thermal and chemical treatments and subsequent drying. (See, e.g., Schena, M. et al. (1995) Science 270:467-470; Shalon, D. et al. (1996) Genome Res. 6:639-645.) Fluorescent probes are prepared and used for hybridization to the elements on the substrate. The substrate is analyzed by procedures described above.

### VIII. Complementary Polynucleotides

Sequences complementary to the HTRM-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring HTRM. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same  
5 procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of HTRM. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the  
10 HTRM-encoding transcript.

### IX. Expression of HTRM

Expression and purification of HTRM is achieved using bacterial or virus-based expression systems. For expression of HTRM in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels  
15 of cDNA transcription. Examples of such promoters include, but are not limited to, the *trp-lac* (*tac*) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria express HTRM upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). Expression of HTRM in eukaryotic cells is achieved by  
20 infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding HTRM by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription.  
25 Recombinant baculovirus is used to infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E. K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

In most expression systems, HTRM is synthesized as a fusion protein with, e.g.,  
30 glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be  
35 proteolytically cleaved from HTRM at specifically engineered sites. FLAG, an 8-amino acid

peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995, *supra*, ch 10 and 16). Purified HTRM obtained  
5 by these methods can be used directly in the following activity assay.

#### X. Demonstration of HTRM Activity

HTRM activity is measured by its ability to stimulate transcription of a reporter gene, essentially as described in Liu, H.Y., et al (1997; EMBO J. 16:5289-5298.). The assay entails the use of a well characterized reporter gene construct, LexA<sub>op</sub>-LacZ, that consists of LexA DNA  
10 transcriptional control elements (LexA<sub>op</sub>) fused to sequences encoding the *E. coli*  $\beta$ -galactosidase enzyme (LacZ). The methods for fusion gene construction, expression, and introduction into cells, and measurement of  $\beta$ -galactosidase enzyme activity, are well known to those skilled in the art. Sequences encoding HTRM are cloned into a plasmid that directs the synthesis of a fusion protein, LexA-HTRM, consisting of HTRM and a DNA binding domain derived from the LexA  
15 transcription factor. The plasmid encoding the LexA-HTRM fusion protein is introduced into yeast cells along with the plasmid containing the LexA<sub>op</sub>-LacZ reporter gene. The amount of  $\beta$ -galactosidase enzyme activity associated with LexA-HTRM transfected cells, relative to control cells, is proportional to the amount of transcription stimulated by the HTRM gene product.

#### 20 XI. Functional Assays

HTRM function is assessed by expressing the sequences encoding HTRM at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT (Life Technologies) and pCR3.1  
25 (Invitrogen, Carlsbad CA), both of which contain the cytomegalovirus promoter. 5-10  $\mu$ g of recombinant vector are transiently transfected into a human cell line, preferably of endothelial or hematopoietic origin, using either liposome formulations or electroporation. 1-2  $\mu$ g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and  
30 is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP, and to evaluate properties, for example, their apoptotic state. FCM detects and quantifies the uptake of fluorescent molecules that diagnose  
35 events preceding or coincident with cell death. These events include changes in nuclear DNA

content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies: and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M. G. (1994) Flow Cytometry, Oxford, New York NY.

The influence of HTRM on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding HTRM and either CD64 or CD64-GFP.

- 10 CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding HTRM and other genes of interest can
- 15 be analyzed by northern analysis or microarray techniques.

## **XII. Production of HTRM Specific Antibodies**

HTRM substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) *Methods Enzymol.* 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

- 20 Alternatively, the HTRM amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel, 1995, supra, ch. 11.)

- 25 Typically, oligopeptides 15 residues in length are synthesized using an ABI 431A Peptide Synthesizer (Perkin-Elmer) using fmoc-chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for
- 30 anti-peptide activity by, for example, binding the peptide to plastic, blocking with 1% BSA. reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

## **XIII. Purification of Naturally Occurring HTRM Using Specific Antibodies**

- Naturally occurring or recombinant HTRM is substantially purified by immunoaffinity chromatography using antibodies specific for HTRM. An immunoaffinity column is constructed
- 35 by covalently coupling anti-HTRM antibody to an activated chromatographic resin, such as

CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

Media containing HTRM are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of HTRM (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/HTRM binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and HTRM is collected.

#### **XIV. Identification of Molecules Which Interact with HTRM**

HTRM, or biologically active fragments thereof, are labeled with  $^{125}\text{I}$  Bolton-Hunter reagent. (See, e.g., Bolton et al. (1973) Biochem. J. 133:529.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled HTRM, washed, and any wells with labeled HTRM complex are assayed. Data obtained using different concentrations of HTRM are used to calculate values for the number, affinity, and association of HTRM with the candidate molecules.

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.

Table 1

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
1	66	001106	U937NOT01	001106 (U937NOT01), 1291142 (BRAINT01), 2590425 (LUNGN022), 1300570 (BRSTNOT07)
2	67	004586	HMC1NOT01	004586 (HMC1NOT01), 389843 (BRSTTUT16), 1432988 (BEPINON01), 788995 (PROSTUT03), 1605475 (LUNGN015)
3	68	052927	FIBRNOT01	052927 (FIBRNOT01), 2518848 (BRAITUT21), 3520218 (LUNGNON03), 086878 (LIVRNOT01)
4	69	082843	HUVESTB01	082843 (HUVESTB01), 4008105 (ENDCNOT04), 2083528 (UTRSNOT08), 2345764 (TESTTUT02), 3771780 (BRSTNOT25), 190782 (CONVTUT01), 2206259 (SPLNFET02), 2509193 (CONVTUT01)
5	70	322349	EOSIHET02	322349 (EOSIHET02), 3686018 (HEARNOT01), 1853592 (LUNGFET03), 815966 (OVARTUT01), 1505002 (BRAITUT07), 1511883 (LUNGN014), 2232826 (PROSN016)
6	71	397663	PITUNOT02	397663 (PITUNOT02), 491141 (HNT2AGT01), 3809879 (CONVTUT01) 3562349 (SKINNOT05), 1518413 (BLADTUT04), 3600151 (DRGTNOT01), 2474103 (THPINOT03), 2105304 (BRAITUT03), 2187330 (PROSN026), 1781572 (PGANNON02), 2056258 (BEPINOT01), 1888065 (BLADTUT07)
7	72	673766	CRBLNOT01	673766 (CRBLNOT01), 2494421 (ADRETUT05), 3267748 (BRAINT020) 2194042 (THRTUT03), 3186455 (THYMNON04), 1712236 (PROSN016) 1844092 (COLANOT08), 1602283 (BLADNOT03), 033357 (THP1NOB01), 1995828 (BRSTTUT03), 1485594 (CORPNOT02)
8	73	1504753	BRAITUT07	1504753 (BRAITUT07), 633939 (NEUTGMT01), 2741379 (BRSTTUT14), 2959661 (ADRENOT09), 3483904 (KIDNNOT31), 999401 (KIDNTUT01), 1965504 (BRSTNOT04), 588535 (UTRSNOT01)
9	74	1760185	PITUNOT03	1760085 (PITUNOT03), 1914471 (PROSTUT04), 836831 (PROSN07), 729798 (LUNGNOT03), 1290847 (BRAINT01), 1492387 (PROSNON01), 1368472 (SCORNON02)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
10	75	1805061	SINTNOT13	1805061 (SINTNOT13), 1435949 (PANCNOT08), 086122 (LIVRNOT01) 1482366 (CORPNOT02), 1835310 (BRAINON01), 1333758 (COLNNOT13), 3521449 (LUNGNON03)
11	76	1850120	LUNGFET03	1850120 (LUNGFET03), 3126350 (LUNGTUT12), 786916 (PROSNOT05) 2899740 (DRGCNOT01), 1259221 (MENITUT03), 1334740 (COLNNOT13), 2466350 (THYRNOT08)
12	77	1852290	LUNGFET03	1852290 (LUNGFET03), 2901081 (DRGCNOT01), 1384842 (BRAITUT08) 1293541 (PGANNOT03), 1964126 (BRSTNOT04)
13	78	1944530	PITUNOT01	1944530 (PITUNOT01), 2808142 and 2809196 (BLADTUT08), 2961779 (ADRENOT09)
14	79	2019742	CONNNOT01	2019742 (CONNNOT01), 2968014 (SCORNOT04), 168472 (LIVRNOT01) 1875993 (LEUKNOT02), 1522480 (BLADTUT04), 1418496 (KIDNNOT09), 149730 (FIBRNGT02)
15	80	2056042	BEPINOT01	2056042 (BEPINOT01), 3097391 (CERVNOT03), 1985203 (LUNGAST01) 1962619 (BRSTNOT04), 1335716 (COLNNOT13)
16	81	2398682	THP1AZT01	2398682 (THP1AZT01), 159706 (ADENINB01), 2443910 (THPINOT03) 2382189 (ISLTNOT01), 2288661 (BRAINON01), 1864422 (PROSNOT19)
17	82	2518753	BRAITUT21	2518753 (BRAITUT21), 4001219 (HMT2AZS07), 2606361 (LUNGTUT07) 449043 (TLYMNOT02), SAEA01390
18	83	2709055	PONSAZT01	2709055 (PONSAZT01), 2309703 (NGANNOT01), 1661042 (URETTUT01), 2761284 (ESOGTUT02), 2469634 (THPINOT03), SBLA03183, SBLA00549 SBLA00975
19	84	2724537	LUNGTUT10	2724537 (LUNGTUT10), 3869823 (BVARNOT03), 952779 (SCORNON01), 2049127 (LIVRFET02), 1824284 (GELATUT01), 1870588 and 1869666 (SKINEIT01), 2626505 (PROSTUT12), SAEA03404, SAEA01744 SAEA01672, SAEA10045, SAPA04072, SAPA00149

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragment
20	85	025818	SPLNFET01	025818H1, 025818X12, and 025818X3 (SPLNFET01), 783259H1 (MYOMNOT01), 826162R1 (PROSNOT06)
21	86	438283	THYRNOT01	438283H1 and 438283X29 (THYRNOT01), SAGA01136F1, SAGA01671F1, SAGA02704F1, SAGA03722F1, SZZZ01038R1
22	87	619699	PGANNOT01	619699H1, 619699X11, and 619699X18 (PGANNOT01), 646198T6 (BRSTTUT02), 1322305X20F1 (BLADNOT04), 1724376F6 (PROSNOT14)
23	88	693452	SYNORAT03	118140R1 (MUSCNOT01), 693452H1 and 693452R6 (SYNORAT03), 2455538F6 and 2455538H1 (ENDANOT01), 4500333H1 (BRAVXTXT02)
24	89	839651	PROSTUT05	729341X12 (LUNGNOT03), 839651CT1, 839651H1, and 839651X55 (PROSTUT05), 839651X60 (PROSTUT05)
25	90	1253545	LUNGFET03	1253545H1 and 1254914F6 (LUNGFET03), 1806337X13F1 and 1807402X11F1 (SINTNOT13), 2179882X22F1 (SININOT01), 2592938F6 (LUNGNOT22), 2840018F6 (DRGLNOT01)
26	91	1425691	BEPINON01	2727135H1 (OVARTUT05), 587126X29R1, 588598X17, and 587126F1 (UTRSNOT01), 1714529F6 (UCMCNOT02), 1381341F6 (BRAITUT08), 1273513F6 (TESTTUT02), 060265R1 (LUNGNOT01), 1459659F1 (COLNFET02), 043139R1 (TBLYNOT01), 1425691H1 (BEPINON01)



Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
27	92	1484257	CORPNOT02	400685H1, 404702F1, 404702R6, 404702X45C1, 404702X47C1, and 404702X48C1 (TMLR3DT01), 1484257H1 (CORPNOT02), 3396312H1 (UTRSNOT16)
28	93	1732368	BRSTTUT08	920006H1 (RATRNOT02), 1732368F6 and 1732368H1 (BRSTTUT08), 2607269T6 (LUNGUTUT07), 2654363F6 (THYMNUT04)
29	94	1870914	SKINBIT01	1549551R6 (PROSNUT06), 1575349H1 (LNODNOT03), 1870914H1 (SKINBIT01), 2365851T6 (ADRENUT07), SBKA00149F1
30	95	1910984	CONNTUT01	859876X12 (BRAITUT03), 1234976H1 and 1241845H1 (LUNGNOT03), 1910984F6 and 1910984H1 (CONNTUT01), 3276505H1 (PROSBPT06)
31	96	1943040	HIPONUT01	824144R1 (PROSNUT06), 930281H1 (CERVNOT01), 1420545H1 (KIDNNOT09), 1784405H1 (BRAINUT10), 1943040H1 and 1943040R6 (HIPONUT01), 2122271H1 (BRSTNOT07), 2729723H1 (OVARTUT04)
32	97	2076520	ISLTNOT01	419755R1 (BRSTNOT01), 954937R1 (KIDNNOT05), 1460268H1 (COLNFET02), 1599016H1 (BLADNOT03), 2076520H1 (ISLTNOT01), 2082255F6 (UTRSNOT08), 2184150F6 (SININUT01), 2884394F6 (SINJNOT02), 3726575H1 (BRSTNOT23), 3752466H1 (UTRSNOT18), 3764971H1 (BRSTNOT24), 4412005H1 (MONOTXT01)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
33	98	2291241	BRAINON01	2291241CT1 and 2291241H1 (BRAINON01), 2500586H1 (ADRETUT05)
34	99	2329692	COLNNOT11	158014F1 (ADENINB01), 1519462F1 (BLADTUT04), 1543875R1 (PROSTUT04), 2329692H1, 2331530R6, and 2331530T6 (COLNNOT11), 2478291F6 (SMCANOT01)
35	100	2474110	THP1NOT03	863265H1 (BRAITUT03), 1313444F1 (BLADTUT02), 1872631T6 and 1872869F6 (LEUKNOT02), 2061219R6 (OVARNOT03), 2171863H1 (ENDCNOT03), 2474110H1 (THP1NOT03), 2690250H1 (LUNGNOT23), 2812791F6 (OVARNOT10)
36	101	2495790	ADRETUT05	1360349T1 (LUNGNOT12), 1689792H1 (PROSTUT10), 1795321H1 (PROSTUT05), 1905521F6 (OVARNOT07), 1907168F6 (OVARNOT07), 2495790H1 (ADRETUT05), 2587542F6 (BRAITUT22)
37	102	2661254	ADRENOT08	1241850H1 (LUNGNOT03), 1545867R1 (PROSTUT04), 2325561H1 (OVARNOT02), 2661254H1 (ADRENOT08), 2751457H1 (THP1AZS08)
38	103	2674047	KIDNNOT19	489330H1 (HNT2AGT01), 2059316R6 (OVARNOT03), 2059316T6 (OVARNOT03), 2674047F6 and 2674047H1 (KIDNNOT19), 2805474H1 (BLADTUT08), 3076605H1 (BONEUNT01), 3080137T6 (BRAIUNT01)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
39	104	2762174	BRAINOS12	2573448T3 (HIPOAZT01), 2762174H1 (BRAINOS12), SBNA00508F1, SBNA01683F1, SBNA00674F1, SBNA00857F1
40	105	2765991	BRSTNOT12	082008R6 (HUVESB01), 2127491T6 (KIDNNOT05), 2765991F6 and 2765991H1 (BRSTNOT12), 3147681H1 (PENCNOT05), SZAH01537F1, SZAH01356F1
41	106	2775157	PANCNOT15	2325410H1 (OVARNOT02), 2506671F6 and 2506671T6 (CONUTUT01), 2775157F6 and 2775157H1 (PANCNOT15), 3376091F6 (PENGNOT01), 3412063H1 (BRSTTUS08)
42	107	2918375	THYMFET03	227782F1 (PANCNOT01), 1225559H1 (COLNTUT02), 1511458T1 (LUNGNOT14), 2918375H1 (THYMFET03)
43	108	3149729	ADRENON04	605315F1 (BRSTTUT01), 3149729CT1 and 3149729H1 (ADRENON04)
44	109	3705895	PENCNOT07	744201R1 (BRAITUT01), 2550322H1 (LUNGUT06), 3705895H1 (PENCNOT07)

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
45	110	003256	HMCINOT01	003256H1, 003256R6, 003256T6, 003256X305F1, 003256X313F, 003256X315F1, and 009404H1 (HMC1NOT01), 43104R1 (TBLYNOT01), 413017F1 (BRSTNOT01)
46	111	156986	THP1PLB02	010084F1 and 012909H1 (THP1PLB01), 156986H1 and 156986R1 (THP1PLB02), 1320255F1 (BLADNOT04), 1512255F1 (LUNGNOT14), 2061923T6 (OVARNOT03), 2398787F6 (THP1AZT01), 2517160H2 (LIVRTUT04)
47	112	319415	EOSIHET02	285773H1, 285773R1, 319415H1, and 319415X19F1 (EOSIHET02), 1231455H1 (BRAITUT01), 1804042F6 (SINTNOT13), 1878858F6 (LEUKNOT03)
48	113	635581	NEUTGMT01	635581H1 (NEUTGMT01), 3045776F6 (HEAANOT01)
49	114	921803	RATRNOT02	921803H1 (RATRNOT02), 1275128T6 (TESTTUT02), 1709959F6 (PROSNOT16), 2416547F6 (HNT3AZT01), 3016146H1 (MUSCNOT07), 3577260H1 (BRONNOT01)
50	115	1250492	LUNGFET03	691921X14F1 (LUNGTUT02), 1250492F6, 1250492H1, and 1252265F2 (LUNGFET03), 1361644F6 (LUNGNOT12), 3049358F6 (LUNGNOT25), 4044523H1 and 4048275H1 (LUNGNOT35), 4145295H1 (SINITUT04)
51	116	1427838	SINTBST01	1261181H1 (SYNORAT05), 1427838H1 and 1427838T1 (SINTBST01), 1733769T6 (BRSTTUT08), 2551854H1 (LUNGTUT06)
52	117	1448258	PLACNOT02	1448258H1 and 1448258R1 (PLACNOT02), 1484126F1 (CORPNOT02), 1856631F6 and 1856631X11F1 (PROSNOT18), 2690070F6 (LUNGNOT23), SAMA00131F1 and SAMA00146F1

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
53	118	1645941	PROSTUT09	831680R6 (PROSTUT04), 1645941F6 and 1645941H1 (PROSTUT09), 1748682F6 (STOMTUT02), 1870831F6 (SKINBIT01), 1877907F6 (LEUKNOT03), 2310427R6 (NGANNOT01)
54	119	1646005	PROSTUT09	1646005H1, 1646005X309F1, 1646005X312F1 and 1646883F6 (PROSTUT09), SZA02276F1
55	120	1686561	PROSNOT15	1234124H1 (LUNGFET03), 1299156F6 (BRSTNOT07), 1425185R1 (BEPINON01), 1544751T1 (PROSTUT04), 1686561H1 (PROSNOT15), 2723108H1 (LUNGUTUT10), 2752156H1 (THP1AZS08), 3335850F6 (BRAIFET01), 3502259H1 (ADRENOT11), 3857461H1 (LNODNOT03), 5069547H1 (PANCNOT23)
56	121	1821233	GBLATUT01	030744H1 (THP1NOB01), 1272043F1 (TESTTUT02), 1419549F1 (KIDNNOT09), 1433773R1 (BEPINON01), 1482848F1 (CORPNOT02), 1821233H1 (GBLATUT01), 1869022H1 (SKINBIT01)
57	122	1877278	LEUKNOT03	1871148F6 (SKINBIT01), 1877278H1 (LEUKNOT03), 2097362T6 (BRAITUT02), 3124246T6 (LNODNOT05), 3450007R6 (UTRSNON03), 4894340H1 (LIVRTUT12), SAE02108R1
58	123	1880692	LEUKNOT03	1880692H1 (LEUKNOT03), SBAA00446F1, SARA03727F1

Table 1 cont.

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
59	124	2280456	PROSNON01	1557906F6 (BLADTUT04), 2280456H1 (PROSNON01), 2799446F6 (NPOLNOT01), 3519009H1 (LUNGNON03)
60	125	2284580	BRAINON01	783560H1 (MYOMNOT01), 1215190T2 (BRSTTUT01), 1458188F1 (COLNFET02), 2284580H1 (BRAINON01), 2398366F6 (THPIAZT01), 2469268H1 (THP1NOT03)
61	126	2779172	OVRTUT03	487548H1 and 487548R6 (HNT2AGT01), 1421684F1 (KIDNNOT09), 2172754F6 (ENDCNOT03), 2672062F6 (ESOGTUT02), 2779172F6 and 2779172H1 (OVRTUT03), 2935502F6 (THYMFET02), 3206879F6 (PENCNOT03)
62	127	3279329	STOMFET02	885282R6 and 885282T1 (PANCNOT05), 901139R1 (BRSTTUT03), 1655530F6 (PROSTUT08), 1818669T6 (PROSNOT20), 2380664F6 (ISLTNOT01), 2921229H1 (SININOT04), 32793329H1 (STOMFET02), 3451425R6 (UTRSNON03)
63	128	3340290	SPLNNOT10	102935H1 (ADRENOR01), 1363193F6 (LUNGNOT12), 1674514H1 (BLADNOT05), 2271374H1 (PROSNON01), 2827770H1 (TLYMNOT03), 3340290H1 (SPLNNOT10), 4556330H1 (KERAUNT01)
64	129	3376404	PENGNOT01	3376404H1, 3376404X300U1, 3376404X310U1, and 3376404X323U1 (PENGNOT01), 3741323X302B1 (MENTNOT01)
65	130	4173111	SINTNOT21	1337315F6 (COLNNOT13), 2486184F6 (CONUTUT01), 4173111H1 (SINTNOT21), 4750042H1 (SMCRUNT01)

Table 2

Protein SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
1	155	S9, S16, T25, S37, S56, S57, S81, S114, T152		G38-I73	sigma-54 interaction protein	BLOCKS
2	152	S6, T83, S103, T121, S136		H99-R112	LUPUS La protein	PRINTS
3	304	S30, S61, S94, T109, S132, S133, T183, T236, S277, S289	N65, N294	C228-C268 C231-I255	zinc finger/RING finger protein	PFAM, BLOCKS
4	178	T8, S48, S102, Y121, T144		N18-P32	histone H3 protein	PRINTS
5	301	T58, T70, T85, S148, T165, S256, T272, S281	N191	K21-F38	filaggrin structural protein	PRINTS
6	250	S99, S126, S142, S155, T182		F203-V214	maspin/breast tumor suppressor protein	PRINTS
7	371	T25, S46, S96, T123, S128, T144, S163, S167, S205, S221, T350	N203, N222, N307, N348	EQ165-Y185 K152-L192	human/leucine zipper/CRE protein	BLAST, BLOCKS, PRINTS

Table 2 cont.

Protein SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
8	148	T35, S41, S92, S105	N144		TSC-22 transcription factor	BLAST
9	127	T69	N53	M1-E16	Ribosomal protein S6	PFAM
10	383	S22, T34, S53, S140, T155, T183, S225, T263, S273, S300, S308, T369, S375	N127	Q7-K112	PH-domain protein	Pfam
11	254	T57, S62, S92, S143, S148, T166, T176, S180, T187, S191, S194, T221			cyclin-dependent-k inase binding protein	BLAST
12	305	S65, T88, S146, S230, S248, S272	N221	G84-N271	ribosomal protein L2	PFAM, BLOCKS
13	230	T34, T49, S54, S122, T123, T150, S182, T209	N86, N130, N199	C155-C191	zinc finger/RING finger protein	PFAM, BLOCKS, MOTIFS
14	292	S2, T61, T89, T193, S223, S224, S225, S238, S288	N47, N101, N166, N259	A124-I145	FOS transforming protein	PRINTS



Table 2 cont.

Protein SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
15	232	T58, S72, S127, S149, T154, S191, S199, T203, T204	N56, N183, N187	E39-F73	tropomyosin	BLOCKS PRINTS
16	376	T5, T34, S53, T70, S81, T86, S105, S256, T287, T288, T310, S331, S364, S369, T365		Q97-C135	RecA DNA repair protein	BLOCKS BLAST
17	204	T100, T118, T157, S187, S199		L179-H200	annexin	PRINTS
18	713	S46, T64, T71, T95, S96, T129, T171, S260, S286, T345, S438, S485, T527, T541, Y567, Y593, S644, T656	N110, N453, N460, N595	L563-L576 L583-I596	RSP-1 /Ras-signaling protein	BLAST, PRINTS
19	360	S22, T51, S69, T106, S133, S206, T232, S248			Nucleolar protein Surf-6	BLAST
20	196	S38 S69 T23 T30 S73 S183 S37 T84	N9 N51	E76-L91 R35-K58	Helix-loop-helix protein HES-1	MOTIFS BLOCKS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
21	540	T136 S34 S69 S189 T322 S411 T7 S66 S75 T139 S193 S197 S205 T285 S324 S328 S380 S425	N240 N443	C230-H252, C260- H280, C288-H309, C316-H336, C344- H364, C372-H392, C400-H420, C428- H448, C456-H476, C484-H504, C512- H532	zinc finger protein	MOTIFS BLAST PRINTS
22	549	S123 S22 S182 T319 T465 S161 T205 S208 S332 S392 S459 S534	N167 N335 N422	C214-H234, C242- H262, C270-H290, C298-H318, C326- H346, C354-H374, C382-H402, C410- H430, C438-H458, C466-H486, C494- H514, C522-H542	zinc finger protein ZNF43	MOTIFS BLAST PRINTS
23	361	S244 T254 S8 S58 S180 S193 T269 T283 S284 T26 S45 S174 T254 S314		C139-L163 C227-K263	DNA binding protein	BLOCKS BLAST
24	241	S82 S62 S119 T147 Y111		C52-H75, C83- H105, C113-H133, C141-H161, C172- H193	zinc finger protein PZF	MOTIFS PRINTS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
25	576	S90 T371 S56 T183 T195 S203 S316 T318 S347 S354 S432 S548 S37 S82 S281 T325 S343 S409 S414 S447 S466 T481 S502 S570 Y323	N42 N312 N339 N498	C507-L543, L168- L189, E262-R278	transcription factor	MOTIFS PRINTS BLOCKS BLAST
26	408	S74 S197 T226 S247 T289 S328 S338 S353 S386 S394 T14 S199 S234 T388	N245 N253	G164-R175	transcription factor	PRINTS BLAST
27	810	S392 S113 S155 S185 S225 S262 S283 T298 S342 S433 T449 T665 T695 S728 T756 T801 T79 T190 S377 T438 Y397		C315-H335, C343- H363, C371-H391, C399-H419, C427- H447, C455-H475, C483-H503, C511- H531, C539-H559, C567-H587, C595- H615, C623-H644, C726-H747	zinc finger protein Miz-1	MOTIFS PRINTS BLOCKS
28	324	S72 T189 S209 T223 S279 S302 S156 T182 S316 Y277	N187	C74-R85	Hormone-binding transcription factor protein	PRINTS BLAST
29	292	S242 T41 S136 S137 T176 T200 S205 S284 T52 S61	N229	G62-S69	putative nucleotide-binding protein	MOTIFS PRINTS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
30	259	T79 S99 S180 T20 S152 S241		C71-H92, C43-C71	zinc finger protein	MOTIFS BLOCKS BLAST
31	97	S52		C15-L43	DNA-binding protein	MOTIFS BLOCKS BLAST
32	812	T239 T16 S55 T56 T104 S126 S127 T156 S176 T249 S268 T269 S330 T394 S450 T484 S583 S652 S658 S795 S33 S235 T314 S343 T730 S804	N45 N93 N165 N805	E418-S450	cell cycle protein	BLOCKS BLAST
33	392	T22 S30 T43 S55 S108 T140 S156 S318 T320 S343 S120 S270 S311	N277		TRAF family member-associated NF-kB activator TANK	BLAST
34	60	T49 T30 S50		I2-S55	DNA-binding protein	BLOCKS BLAST
35	209	S21 S57 T93	N67	F160-N179 S151-G185	cellular nucleic acid binding protein	PRINTS BLOCKS BLAST
36	257	T178 S187 S230 T249	N65	Y33-F44 S187-L205	cell-cycle control protein Hst2p	PRINTS BLOCKS BLAST

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
37	138	T106 T3 S27 S46		E108-Q124	nucleic acid- binding protein	BLOCKS BLAST
38	999	T54 S634 S89 S126 S335 S414 S442 S451 T512 T762 T792 T858 S890 T97 T994 T205 S233 T274 T491 S525 S534 T577 T600 S610 S615 S634 S677 T951 S961 Y152 Y458 Y686 Y815	N43 N532 N672 N749 N818 N943	L574-L595 L647-L668	DNA-binding protein	MOTIFS BLAST
39	377	T142 T254 T48 T138 S292 S71 S74 S108 S114 T138 S222 S250 T332 T364		C130-H150, C158- H178, C186-H206, C214-H234, C242- H262, C270-H290, C296-H316, C324- H344, C352-H372	zinc finger protein ZNF132	MOTIFS PRINTS BLOCKS BLAST
40	324	S28 S214 S16 S81 S114 T225 T33 S44 T66 S203 S209 T229	N47	R26-S37 S77-L115	transcription regulatory protein IRLB	PRINTS BLOCKS BLAST
41	270	S16 T123 T141 T199 S9 S52 S90 T128 T175 S194 S214	N22 N109 N192	V218-L242 P250-Q263		MOTIFS BLOCKS PRINTS

Table 2 cont.

Protein Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
42	252	T20 S48 S89 S101 T127 S218 T121 S126 T152	N33 N46 N216 N230	Y9-L18, S68-F88, D159-S168	cell-cycle control protein	PRINTS BLAST
43	228	T50 T107 T2 S42 S201 T31 S51 T52 T103 T107 T134 T143 T206 S210 T215	N132 N141 N165 N197	A38-S51, Q65- P100, S59-K89	Transcriptional Repressor Protein	PRINTS BLOCKS BLAST
44	117	T93 T11		A86-E104	CCAAT-Binding Transcription factor	PRINTS BLAST
45	252	S83 T2 S57 T159 S250 Y102	N197	M1-S29 A85-K123	Ribosomal protein	BLOCKS MOTIFS
46	530	T177 S234 S461 S519 T24 T238	N217 N227	TM Domains: Y147-A167 Y242-L262 L306-F325 L332-L351 S379-F399 L470-F489	melibiose carrier protein	BLAST MOTIFS HMM

Table 2 cont.

SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
47	355	S7 S21 T127 S213 T279 S134 T276 S315 S331 S334 Y193 Y300	N37 N192 N263 N268 N337	I42-E69 W160-E187 G171-G200 N234-I256	Myelin P0 Protein	BLOCKS, PRINTS MOTIFS, IMM
48	136	T109 S130 T5 T69 T40 S121			geminin	BLAST, MOTIFS
49	235	T138 T142 S180 S230 S111 S120 S137 T224	N140 N198	ATP/GTP binding: G9-T16	PTB-associated splicing factor	BLAST MOTIFS
50	70	T2 S64			ninjurin	BLAST MOTIFS
51	169	T128 T26 S96			B locus M Beta chain 1	BLAST, MOTIFS
52	359	S55 S78 T161 S245 T292 T350 T57 T130 T289	N105	E205-S242 E271-V294	ribosomal protein S6 kinase 2	BLAST, MOTIFS BLOCKS, PRINTS, PFAM
53	545	S235 T317 S47 S73 S114 S146 S184 S236 S241 S394 S538 S2 T84 S109 S124 T230 S231 S266 S340 T360 S379 S525	N45 N139 N431 N478 N511	K88-I106 A333-K362	ribosomal protein	MOTIFS BLOCKS PRINTS

Table 2 cont.

SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
54	99	T90 T43 T76			ORF E4	BLAST, MOTIFS
55	565	S27 S56 S132 T152 T197 S319 T411 T429 S475 T66 S156 S303 T390 S463 Y549	N2 N55 N165		Sec1 precursor	BLAST, MOTIFS
56	197	S65 T23 S102 S19 T60 T61 S136 S147	N20		Regulatory protein	BLAST, MOTIFS
57	321	S91 S119 T139 S283 S147 T300 Y238	N103 N194		putative ras effector Norel	BLAST, MOTIFS
58	356	T45 S85 S93 S95 T103 S114 T142 S168 T317 S340 S49 S58 T236 S258 S314 Y12 Y296	N91 N312		weak similarity to S. cerevisiae intracellular transport protein	BLAST MOTIFS
59	299	S273 T81 S116 S120 T122 S146 S86 S151 T210 S225 T268			P13 Kinase P85 Regulator	MOTIFS, PRINTS
60	293	T34 S218 S247 S290 S291 T240 S79 S145 T156 T199 S204 S283	N152	V47-V71 K86-F93	RNA-binding protein	BLAST, MOTIFS BLOCKS, PFAM



Table 2 cont.

Seq ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential glycosylation sites	Signature Sequence	Identification	Analytical Methods
61	777	S81 S128 S141 T230 S315 S342 S352 T519 S564 S576 S684 T699 T758 T205 S213 S236 S294 S397 T417 S470 S515 T560 S640 T746	N228 N281 N319 N453 N481 N636 N682		Zinc finger helicase	BLAST, MOTIFS
62	97	T83		C20-C28	ferredoxin	MOTIFS
63	308	S15 S81 T97 T102 S103 S135 S200 S238 S28 S131 T154 S171 S186 Y232	N58 N78 N95 N198 N236		ubiquitin- conjugating enzyme	BLAST, MOTIFS
64	290	S121 S165 S167 S248 S17 T188 T207 Y86 Y203	N55 N79	M1-A22 C60-C76 C225-C235 W249-I272	prostasin	BLAST, MOTIFS, BLO CKS, PRINTS PFAM, HMM
65	198	S7 S9 S56 T115 T34 T86	N183		transcriptional regulator	BLAST MOTIFS

TABLE 3

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
66	Nervous (0.256) Reproductive (0.209)	Cancer (0.442), Inflammation (0.279), Proliferative/Fetal (12%)	pBlueScript
67	Reproductive (0.274) Cardiovascular (0.194)	Cancer (0.484), Inflammation (0.145), Proliferative/Fetal (0.194)	pBlueScript
68	Reproductive (0.231) Cardiovascular (0.205)	Cancer (0.385), Inflammation (0.231), Proliferative/Fetal (0.205)	pBlueScript
69	Reproductive (0.215) Hematopoietic/Immune (0.190)	Cancer (0.397), Inflammation (0.314), Proliferative/Fetal (0.215)	pBlueScript
70	Reproductive (0.367) Cardiovascular (0.122)	Cancer (0.489), Inflammation (0.233), Proliferative/Fetal (0.189)	pBlueScript
71	Reproductive (0.292) Nervous (0.142)	Cancer (0.469), Inflammation (0.257), Proliferative/Fetal (0.177)	pSPORT1
72	Reproductive (0.261) Nervous (0.157)	Cancer (0.493), Inflammation (0.194), Trauma (0.142)	pSPORT1
73	Reproductive (0.343) Hematopoietic/Immune (0.200)	Cancer (0.457), Inflammation (0.257), Trauma (0.229)	pINCY
74	Reproductive (0.320) Nervous (0.160)	Cancer (0.507), Inflammation (0.187), Proliferative/Fetal (0.133)	pSPORT1
75	Gastrointestinal (0.300) Nervous (0.250)	Cancer (0.400), Inflammation (0.300)	pINCY
76	Reproductive (0.262) Nervous (0.180)	Cancer (0.443), Inflammation (0.262), Proliferative/Fetal (0.230)	pINCY
77	Reproductive (0.283) Nervous (0.151)	Cancer (0.509), Inflammation (0.208), Trauma (0.132)	pINCY

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
78	Cardiovascular (0.300) Nervous (0.200)	Cancer (0.450), Inflammation (0.200)	pBlueScript
79	Reproductive (0.270) Cardiovascular (0.150)	Cancer (0.440), Inflammation (0.180), Proliferative/Fetal (0.150)	pINCY
80	Reproductive (0.271) Cardiovascular (0.153)	Cancer (0.506), Inflammation (0.176), Proliferative/Fetal (0.188)	pSPORT1
81	Hematopoietic/Immune (0.312) Reproductive (0.219)	Cancer (0.344), Inflammation (0.344), Proliferative/Fetal (0.281)	pINCY
82	Nervous (0.250) Hematopoietic/Immune (0.188)	Cancer (0.500), Inflammation (0.438), Proliferative/Fetal (0.188)	pINCY
83	Hematopoietic/Immune (0.276) Reproductive (0.276)	Cancer (0.552), Inflammation (0.310)	pINCY
84	Reproductive (0.309) Nervous (0.144)	Cancer (0.526), Inflammation (0.247), Proliferative/Fetal (0.134)	pINCY
85	Reproductive (0.315) Nervous (0.152) Cardiovascular (0.130)	Cancer (0.522) Fetal (0.174) Inflammation (0.141)	pBLUESCRIPT
86	Reproductive (0.545) Hematopoietic/Immune (0.182) Gastrointestinal (0.182)	Cancer (0.636) Fetal (0.273) Inflammation (0.182)	pBLUESCRIPT
87	Reproductive (0.218) Nervous (0.200) Hematopoietic/Immune (0.200)	Cancer (0.509) Inflammation (0.236) Fetal (0.164)	pSPORT1
88	Nervous (0.296) Reproductive (0.185) Hematopoietic/Immune (0.148)	Cancer (0.407) Fetal (0.259) Inflammation (0.222)	pSPORT1

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
89	Reproductive (0.339) Nervous (0.161) Gastrointestinal (0.145) Cardiovascular (0.145)	Cancer (0.613) Fetal (0.145) Inflammation (0.129)	pSPORT1
90	Cardiovascular (0.278) Gastrointestinal (0.204) Reproductive (0.185)	Cancer (0.519) Inflammation (0.204) Fetal (0.148)	pINCY
91	Reproductive (0.228) Nervous (0.149) Gastrointestinal (0.146)	Cancer (0.411) Inflammation (0.343) Fetal (0.240)	pT7T3
92	Reproductive (0.240) Hematopoietic/Immune (0.160) Gastrointestinal (0.160)	Cancer (0.460) Inflammation (0.260) Fetal (0.180)	pINCY
93	Reproductive (0.333) Cardiovascular (0.200) Hematopoietic/Immune (0.133)	Inflammation (0.533) Cancer (0.400) Fetal (0.133)	pINCY
94	Reproductive (0.230) Gastrointestinal (0.164) Cardiovascular (0.115) Hematopoietic/Immune (0.115)	Cancer (0.443) Inflammation (0.442) Fetal (0.197)	pINCY
95	Reproductive (0.333) Cardiovascular (0.167) Gastrointestinal (0.167)	Cancer (0.750) Inflammation (0.250)	pINCY
96	Reproductive (0.369) Nervous (0.215) Hematopoietic/Immune (0.108) Gastrointestinal (0.108)	Cancer (0.508) Inflammation (0.231) Fetal (0.108)	pBLUESCRIPT
97	Reproductive (0.321) Gastrointestinal (0.179) Hematopoietic/Immune (0.161)	Inflammation (0.411) Cancer (0.393) Fetal (0.161)	pINCY
98	Reproductive (0.205) Nervous (0.192) Cardiovascular (0.164)	Cancer (0.452) Inflammation (0.342) Fetal (0.178)	pSPORT1

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
99	Gastrointestinal (0.423) Reproductive (0.115)	Cancer (0.385) Inflammation (0.288) Fetal (0.173)	pSPORT1
100	Reproductive (0.281) Hematopoietic/Immune (0.234) Nervous (0.141)	Cancer (0.375) Fetal (0.312) Inflammation (0.312)	pINCY
101	Reproductive (0.294) Nervous (0.196) Gastrointestinal (0.118)	Cancer (0.529) Fetal (0.255)	pINCY
102	Reproductive (0.217) Nervous (0.163) Cardiovascular (0.141)	Cancer (0.435) Inflammation (0.174) Fetal (0.152)	pINCY
103	Reproductive (0.263) Hematopoietic/Immune (0.158) Musculoskeletal (0.158)	Cancer (0.526) Inflammation (0.263) Fetal (0.158)	pINCY
104	Nervous (0.400) Reproductive (0.300)	Cancer (0.400) Inflammation (0.300)	pSPORT1
105	Reproductive (0.375) Cardiovascular (0.125) Urologic (0.125)	Cancer (0.500) Inflammation (0.250) Fetal (0.208)	pINCY
106	Gastrointestinal (0.400) Reproductive (0.400) Developmental (0.100) Hematopoietic/Immune (0.100)	Cancer (0.600) Fetal (0.200) Inflammation (0.200)	pINCY
107	Reproductive (0.278) Gastrointestinal (0.152) Nervous (0.139)	Cancer (0.418) Inflammation (0.241) Fetal (0.165)	>pINCY
108	Reproductive (0.364) Hematopoietic/Immune (0.182) Nervous (0.167)	Inflammation (0.409) Cancer (0.364) Fetal (0.136)	pSPORT1

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
109	Nervous (0.227) Reproductive (0.205) Cardiovascular (0.136) Urologic (0.136) Gastrointestinal (0.136)	Cancer (0.568) Inflammation (0.182) Fetal (0.136)	pINCY
110	Hematopoietic/Immune (0.400) Urologic (0.400) Reproductive (0.200)	Cell proliferation (0.800) Inflammation (0.800)	pBluescript
111	Gastrointestinal (0.213) Hematopoietic/Immune (0.191) Nervous (0.191)	Cell proliferation (0.744) Inflammation (0.489)	pBluescript
112	Hematopoietic/Immune (0.405) Gastrointestinal (0.167) Cardiovascular (0.119)	Inflammation (0.619) Cell proliferation (0.381)	pBluescript
113	Hematopoietic/Immune (0.667) Cardiovascular (0.333)	Inflammation (1.000)	pSPORT1
114	Cardiovascular (0.412) Nervous (0.235) Musculoskeletal (0.118)	Cell proliferation (0.765) Inflammation (0.353)	pSPORT1
115	Cardiovascular (0.548) Reproductive (0.161) Developmental (0.129)	Cell proliferation (0.806) Inflammation (0.226)	pINCY
116	Reproductive (0.267) Cardiovascular (0.233) Hematopoietic/Immune (0.233)	Cell proliferation (0.467) Inflammation (0.500)	pINCY
117	Reproductive (0.400) Cardiovascular (0.167) Gastrointestinal (0.133)	Cell proliferation (0.600) Inflammation (0.267)	pINCY
118	Nervous (0.205) Reproductive (0.205) Other (0.154)	Cell proliferation (0.461) Inflammation (0.385)	pINCY
119	Reproductive (0.500) Nervous (0.167) Hematopoietic/Immune (0.167)	Cancer (0.500) Inflammation (0.167) Neurological (0.167)	pINCY

TABLE 3 cont.

Nucleotide Seq ID NO:	Tissue Expression (Fraction of Total)	Disease Class (Fraction of Total)	Vector
120	Reproductive (0.396) Cardiovascular (0.125) Musculoskeletal (0.125)	Cell proliferation (0.750) Inflammation (0.209)	pINCY
121	Reproductive (0.248) Hematopoietic/Immune (0.194) Gastrointestinal (0.147)	Cell Proliferation (0.651) Inflammation (0.380)	pINCY
122	Nervous (0.264) Cardiovascular (0.132) Reproductive (0.132)	Cell proliferation (0.547) Inflammation (0.396)	pINCY
123	Reproductive (0.242) Nervous (0.152) Urologic (0.152)	Cell proliferation (0.788) Inflammation (0.303)	pINCY
124	Nervous (0.333) Cardiovascular (0.167) Hematopoietic/Immune (0.167)	Cell proliferation (0.667) Inflammation (0.500)	pSPORT1
125	Reproductive (0.290) Cardiovascular (0.161) Hematopoietic/Immune (0.113)	Cell proliferation (0.709) Inflammation (0.306)	pSPORT1
126	Reproductive (0.360) Nervous (0.120) Urologic (0.100)	Cell proliferation (0.680) Inflammation (0.320)	pINCY
127	Reproductive (0.364) Gastrointestinal (0.145) Nervous (0.145)	Cell proliferation (0.600) Inflammation (0.400)	pINCY
128	Cardiovascular (0.154) Gastrointestinal (0.154) Reproductive (0.154)	Cell proliferation (0.616) Inflammation (0.308)	pINCY
129	Urologic (1.000)	Cancer (1.000)	pINCY
130	Hematopoietic/Immune (0.214) Cardiovascular (0.143) Gastrointestinal (0.143)	Cell proliferation (0.428) Inflammation (0.357)	pINCY

TABLE 4

Protein SEQ ID NO:	Clone ID	Library	Library Comment
1	001106	U937NOT01	U937NOT01 Library was constructed at Stratagene (STR937207) using RNA isolated from U937 monocyte-like cell line (ATCC CRL1593) established from malignant cells obtained from the pleural effusion of a 37-year-old Caucasian male with diffuse histiocytic lymphoma.
2	004586	HMC1NOT01	HMC1NOT01 Library was constructed using RNA isolated from HMC-1 human mast cell line derived from a 52-year-old female. Patient history included mast cell leukemia. Family history included atherosclerotic coronary artery disease, a joint disorder involving multiple joints, cerebrovascular disease, and diabetes insipidus.
3	052927	FIBRNOT01	FIBRNOT01 Library was constructed at Stratagene (STR937212) using RNA isolated from the WI38 lung fibroblast cell line derived from a 3-month-old Caucasian female fetus.
4	082843	HUVSTB01	HUVSTB01 Library was constructed using RNA isolated from shear-stressed HUV-EC-C (ATCC CRL 1730), an endothelial cell line derived from the vein of a normal human umbilical.
5	322349	EOSIHET02	EOSIHET02 Library was constructed using RNA isolated from peripheral blood cells apheresed from a 48-year-old Caucasian male. Patient history included hypereosinophilia.
6	397663	PITUNOT02	PITUNOT02 Library was constructed using RNA (Clontech 6584-1) isolated from the pituitary gland of 87 male and female donors, 15 to 75 years old.
7	673766	CRBLNOT01	CRBLNOT01 Library was constructed using RNA isolated from cerebellum tissue of a 69-year-old Caucasian male, who died from chronic obstructive pulmonary disease. Patient history included heart failure, myocardial infarction, hypertension, osteoarthritis, and tobacco use.



TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
8	1504753	BRAITUT07	BRAITUT07 Library was constructed using RNA isolated from left frontal lobe tumor tissue removed from the brain of a 32-year-old Caucasian male during excision of a cerebral meningeal lesion. Pathology indicated low grade desmoplastic neuronal neoplasm. Family history included atherosclerotic coronary artery disease.
9	1760185	PITUNOT03	PITUNOT03 Library was constructed using RNA isolated from pituitary tissue of a 46-year-old Caucasian male who died from colon cancer. Patient history included arthritis and peptic ulcer disease.
10	1805061	SINTNOT13	SINTNOT13 Library was constructed using RNA isolated from ileum tissue removed from a 25-year-old Asian female during a partial colectomy and temporary ileostomy. Pathology indicated moderately active chronic ulcerative colitis involving colonic mucosa from the distal margin to the ascending colon. Family history included hyperlipidemia, depressive disorder, malignant cervical neoplasm, and viral hepatitis A.
11	1850120	LUNGFET03	LUNGFET03 Library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus who died at 20 weeks' gestation.
12	1852290	LUNGFET03	The mother was given seven days of erythromycin treatment for bronchitis during the first trimester.
13	1944530	PITUNOT01	PITUNOT01 Library was constructed using RNA (Clontech 6584-2) isolated from the normal pituitary glands of 18 male and female Caucasian donors, 16 to 70 years old, who died from trauma.
14	2019742	CONNNOT01	CONNNOT01 Library was constructed using RNA isolated from mesentery fat tissue removed from a 71-year-old Caucasian male during a partial colectomy and permanent colostomy. Patient history included a cholecystectomy, viral hepatitis, and a hemangioma. Family history included atherosclerotic coronary artery disease, myocardial infarction, and extrinsic asthma.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
15	2056042	BEPINOT01	BEPINOT01 Library was constructed using RNA isolated from a bronchial epithelium (NHBE) primary cell line derived from a 54-year-old Caucasian male.
16	2398682	THP1AZT01	THP1AZT01 Library was constructed using RNA isolated from THP-1 promonocyte cells treated for three days with 0.8 micromolar 5-aza-2'-deoxycytidine. THP-1 (ATCC TIB 202) is a human promonocyte line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.
17	2518753	BRAITUT21	BRAITUT21 Library was constructed using RNA isolated from brain tumor tissue removed from the midline frontal lobe of a 61-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated subfrontal meningothelial meningioma with no atypia. Patient history included depressive disorder; family history included cerebrovascular disease, senile dementia, hyperlipidemia, benign hypertension, atherosclerotic coronary artery disease, and congestive heart failure.
18	2709055	PONSAZT01	PONSAZT01 Library was constructed using polyA RNA isolated from diseased pons tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.
19	2724537	LUNGTUT10	LUNGTUT10 Library was constructed using RNA isolated from lung tumor tissue removed from the left upper lobe of a 65-year-old Caucasian female during a segmental lung resection. Pathology indicated a metastatic grade 2 myxoid liposarcoma and metastatic grade 4 liposarcoma. Patient history included soft tissue cancer, breast cancer, and secondary lung cancer. Family history included benign hypertension.
20	025818	SPLNFET01	SPLNFET01 Library was constructed at Stratagene using RNA isolated from a pool of fetal spleen tissue. 2x10 <sup>6</sup> primary clones were amplified to stabilize the library for long-term storage. Amplification may significantly skew sequence abundances.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
21	438283	THYRNOT01	THYRNOT01 Library was constructed using RNA isolated from thyroid tissue removed from a 64-year-old Caucasian female who died from congestive heart failure.
22	619699	PGANNOT01	PGANNOT01 Library was constructed using RNA isolated from paraganglionic tumor tissue removed from the intra-abdominal region of a 46-year-old Caucasian male during exploratory laparotomy. Pathology indicated a benign paraganglioma and was associated with a grade 2 renal cell carcinoma, clear cell type, which did not penetrate the capsule. Surgical margins were negative for tumor.
23	693452	SYNORAT03	SYNORAT03 Library was constructed using RNA isolated from the wrist synovial membrane tissue of a 56-year-old female with rheumatoid arthritis.
24	839651	PROSTUT05	PROSTUT05 Library was constructed using RNA isolated from prostate tumor tissue removed from a 69-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenocarcinoma (Gleason grade 3+4). Adenofibromatous hyperplasia was also present. Family history included congestive heart failure, multiple myeloma, hyperlipidemia, and rheumatoid arthritis.
25	1253545	LUNGFET03	LUNGFET03 Library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus who died at 20 weeks' gestation.
26	1425691	BEPINON01	BEPINON01 normalized bronchial epithelium library was constructed from 5.12 million independent clones from the BEPINOT01 library. RNA was made from a bronchial epithelium primary cell line derived from a 54-year-old Caucasian male. The normalization and hybridization conditions were adapted from Soares et al., PNAS (1994) 91:9228, using a longer (24-hour) reannealing hybridization period.
27	1484257	CORPNOT02	CORPNOT02 Library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
28	1732368	BRSTTUT08	BRSTTUT08 Library was constructed using RNA isolated from breast tumor tissue removed from a 45-year-old Caucasian female during unilateral extended simple mastectomy. Pathology indicated invasive nuclear grade 2-3 adenocarcinoma, ductal type, with 3 of 23 lymph nodes positive for metastatic disease. Greater than 50% of the tumor volume was in situ, both comedo and non-comedo types. Immunostains were positive for estrogen/progesterone receptors, and uninvolved tissue showed proliferative changes. The patient concurrently underwent a total abdominal hysterectomy. Patient history included valvuloplasty of mitral valve without replacement, rheumatic mitral insufficiency, and rheumatic heart disease. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.
29	1870914	SKINBIT01	SKINBIT01 Library was constructed using RNA isolated from diseased skin tissue of the left lower leg. Patient history included erythema nodosum of the left lower leg.
30	1910984	CONNTUT01	CONNTUT01 Library was constructed using RNA isolated from a soft tissue tumor removed from the clival area of the skull of a 30-year-old Caucasian female. Pathology indicated chondroid chordoma with neoplastic cells reactive for keratin.
31	1943040	HIPONOT01	HIPONOT01 Library was constructed using RNA isolated from the hippocampus tissue of a 72-year-old Caucasian female who died from an intracranial bleed. Patient history included nose cancer, hypertension, and arthritis.
32	2076520	ISLTNOT01	ISLTNOT01 Library was constructed using RNA isolated from a pooled collection of pancreatic islet cells.
33	2291241	BRAINON01	BRAINON01 Library was constructed and normalized from 4.88 million independent clones from the BRAINOT03 library. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
34	2329692	COLNNOT11	COLNNOT11 The COLNNOT11 library was constructed using RNA isolated from colon tissue removed from a 60-year-old Caucasian male during a left hemicolectomy.
35	2474110	THPINOT03	THPINOT03 Library was constructed using RNA isolated from untreated THP-1 cells (ATCC TIB 202), a human promonocyte line derived from the peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.
36	2495790	ADRETUT05	ADRETUT05 Library was constructed using RNA isolated from adrenal tumor tissue removed from a 52-year-old Caucasian female during a unilateral adrenalectomy. Pathology indicated a pheochromocytoma.
37	2661254	ADRENOT08	ADRENOT08 PINCY Library was constructed using RNA isolated from adrenal tissue removed from a 20-year-old Caucasian male, who died from head trauma.
38	2674047	KIDNNOT19	KIDNNOT19 PINCY Library was constructed using RNA isolated from kidney tissue removed a 65-year-old Caucasian male during an exploratory laparotomy and nephroureterectomy. Pathology for the associated tumor tissue indicated a grade 1 renal cell carcinoma within the upper pole of the left kidney. Patient history included malignant melanoma of the abdominal skin, benign neoplasm of colon, cerebrovascular disease, and umbilical hernia. Family history included cardiovascular disease, and cerebrovascular disease, and prostate cancer.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
39	2762174	BRAINOS12	BRAINOS12 pSPORT1 Library was constructed from 4.9 million clones from the BRAINOT03 library by subtraction of abundantly expressed clone pools. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.
40	2765991	BRSTNOT12	BRSTNOT12 pINCY Library was constructed using RNA isolated from diseased breast tissue removed from a 32-year-old Caucasian female during a bilateral reduction mammoplasty. Pathology indicated nonproliferative fibrocystic disease. Family history included benign hypertension and atherosclerotic coronary artery disease.
41	2775157	PANCNOT15	PANCNOT15 pINCY Library was constructed using RNA isolated from diseased pancreatic tissue removed from a 15-year-old Caucasian male during a exploratory laparotomy with distal pancreatectomy and total splenectomy. Pathology indicated islet cell hyperplasia. Family history included prostate cancer and cardiovascular disease.
42	2918375	THYMFET03	THYMFET03 Library was constructed using RNA isolated from thymus tissue removed from a Caucasian male fetus.
43	3149729	ADRENON04	ADRENON04 normalized adrenal gland library was constructed from 1.36 million independent clones from an adrenal tissue library. Starting RNA was made from adrenal gland tissue removed from a 20-year-old Caucasian male who died from head trauma. The library was normalized in two rounds using conditions adapted from Soares et al. (PNAS (1994) 91:9228-9232) and Bonaldo et al. (Genome Res (1996) 6: 791-806) and a significantly longer (48-hours/round) reannealing hybridization period.
44	3705895	PENCNOT07	PENCNOT07 Library was constructed using RNA isolated from penis right corpora cavernosa tissue removed from a male.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
45	003256	HMC1NOT01	HMC1NOT01 library was constructed using RNA isolated from the HMC-1 human mast cell line derived from a 52-year-old female. Patient history included mast cell leukemia.
46	156986	THP1PLB02	THP1PLB02 library was constructed by reamplification of THP1PLB01, which was made using RNA isolated from THP-1 cells cultured for 48 hours with 100 ng/ml phorbol ester (PMA), followed by a 4-hour culture in media containing 1 ug/ml LPS. THP-1 (ATCC TIB 202) is a human promonocyte line derived from the peripheral blood of a 1-year-old male with acute monocytic leukemia (ref: Int. J. Cancer (1980) 26:171).
47	319415	EOSIHET02	EOSIHET02 library was constructed using RNA isolated from peripheral blood cells adhered from a 48-year-old Caucasian male. Patient history included hypereosinophilia. The cell population was determined to be greater than 77% eosinophils by Wright's staining.
48	635581	NEUTGMT01	NEUTGMT01 library was constructed using RNA isolated from peripheral blood granulocytes collected by density gradient centrifugation through Ficoll-Hypaque. The cells were isolated from buffy coat units obtained from 20 unrelated male and female donors. Cells were cultured in 10 nM GM-CSF for 1 hour before washing and harvesting for total RNA preparation.
49	921803	RATRN02	RATRN02 library was constructed using RNA isolated from the right atrium tissue of a 39-year-old Caucasian male, who died from a gunshot wound.
50	1250492	LUNGFET03	LUNGFET03 library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.
51	1427838	SINTBST01	SINTBST01 library was constructed using RNA isolated from ileum tissue obtained from an 18-year-old Caucasian female during bowel anastomosis. Pathology indicated Crohn's disease of the ileum, involving 15 cm of the small bowel. Family history included cerebrovascular disease and atherosclerotic coronary artery disease.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
52	1448258	PLACNOT02	PLACNOT02 library was constructed using RNA isolated from the placental tissue of a Hispanic female fetus, who was prematurely delivered at 21 weeks' gestation. Serologies of the mother's blood were positive for CMV (cytomegalovirus).
53	1645941	PROSTUT09	PROSTUT09 library was constructed using RNA isolated from prostate tumor tissue removed from a 66-year-old Caucasian male during a radical prostatectomy, radical cystectomy, and urinary diversion. Pathology indicated grade 3 transitional cell carcinoma. The patient presented with prostatic inflammatory disease. Patient history included lung neoplasm and benign hypertension. Family history included a malignant breast neoplasm, tuberculosis, cerebrovascular disease, atherosclerotic coronary artery disease and lung cancer.
54	1646005	PROSTUT09	PROSTUT09 library was constructed using RNA isolated from prostate tumor tissue removed from a 66-year-old Caucasian male during a radical prostatectomy, radical cystectomy, and urinary diversion. Pathology indicated grade 3 transitional cell carcinoma. The patient presented with prostatic inflammatory disease. Patient history included lung neoplasm and benign hypertension. Family history included a malignant breast neoplasm, tuberculosis, cerebrovascular disease, atherosclerotic coronary artery disease and lung cancer.
55	1686561	PROSNOT15	PROSNOT15 library was constructed using RNA isolated from diseased prostate tissue removed from a 66-year-old Caucasian male during radical prostatectomy and regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 2+3). The patient presented with elevated prostate specific antigen (PSA). Family history included prostate cancer, secondary bone cancer, and benign hypertension.



TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
56	1821233	GBLATUT01	The GBLATUT01 library was constructed using RNA isolated from gallbladder tumor tissue removed from a 78-year-old Caucasian female during a cholecystectomy. Pathology indicated invasive grade 2 squamous cell carcinoma, forming a mass in the gallbladder. Patient history included diverticulitis of the colon, palpitations, benign hypertension, and hyperlipidemia. Family history included a cholecystectomy, atherosclerotic coronary artery disease, atherosclerotic coronary artery disease, hyperlipidemia, and benign hypertension.
57	1877278	LEUKNOT03	The LEUKNOT03 library was constructed using RNA isolated from white blood cells of a 27-year-old female with blood type A+. The donor tested negative for cytomegalovirus (CMV).
58	1880692	LEUKNOT03	The LEUKNOT03 library was constructed using RNA isolated from white blood cells of a 27-year-old female with blood type A+. The donor tested negative for cytomegalovirus (CMV).
59	2280456	PROSNON01	The PROSNON01 library was constructed and normalized from 4.4 Million independent clones from the PROSNOT11 library. RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a self-inflicted gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.
60	2284580	BRAINON01	The BRAINON01 library was constructed and normalized from 4.88 million independent clones from the BRAINOT03 library. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.

TABLE 4 cont.

Protein SEQ ID NO:	Clone ID	Library	Library Comment
61	2779172	OVARTUT03	OVARTUT03 library was constructed using RNA isolated from ovarian tumor tissue removed from the left ovary of a 52-year-old mixed ethnicity female during a total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal and lymphatic structure biopsy, regional lymph node excision, and peritoneal tissue destruction. Pathology indicated an invasive grade 3 (of 4) seroanaplastic carcinoma forming a mass in the left ovary. Patient history included breast cancer, chronic peptic ulcer, and joint pain. Family history included colon cancer, cerebrovascular disease, breast cancer, type II diabetes, esophagus cancer, and depressive disorder.
62	3279329	STOMFET02	STOMFET02 library was constructed using RNA isolated from stomach tissue removed from a Hispanic male fetus, who died at 18 weeks' gestation.
63	3340290	SPLNNOT10	SPLNNOT10 library was constructed using RNA isolated from spleen tissue removed from a 59-year-old Caucasian male during a total splenectomy and exploratory laparotomy. Pathology for the spleen indicated splenomegaly with congestion. The lymph nodes showed reactive follicular hyperplasia. The liver showed mild, nonspecific steatosis. The patient presented with abdominal pain, bloating of the abdomen, low-grade fever, and diaphoresis. Family history included myocardial infarction, arteriosclerotic cardiovascular disease, primary tuberculous infection, cerebrovascular disease and lymphoma.
64	3376404	PENGNOT01	PENGNOT01 library was constructed using RNA isolated from glans tissue removed from the penis of a 3-year-old Black male. Pathology for the associated tumor tissue indicated invasive grade 4 urothelial carcinoma forming a soft tissue scrotal mass that invaded the cavernous body of the penis and encased both testicles.
65	4173111	SINTNOT21	SINTNOT21 library was constructed using RNA isolated from small intestine tissue obtained from a 8-year-old Black male, who died from anoxia. Serology was negative.

Table 5

Program	Description	Reference	Parameter Threshold
ABI FACTURA	A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA.	
ABI/PARACEL FDF	A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.	Mismatch <50%
ABI AutoAssembler	A program that assembles nucleic acid sequences.	Perkin-Elmer Applied Biosystems, Foster City, CA.	
BLAST	A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.	Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25: 3389-3402.	ESTs: Probability value= 1.0E-8 or less Full Length sequences: Probability value= 1.0E-10 or less
FASTA	A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises at least five functions: fasta, tfasta, fastx, tfastx, and ssearch.	Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad. Sci. 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183: 63-98; and Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489.	ESTs: fasta E value=1.06E-6 Assembled ESTs: fasta Identity= 95% or greater and Match length=200 bases or greater; fastx E value=1.0E-8 or less Full Length sequences: fastx score=100 or greater
BLIMPS	A BLocks IMProved Searcher that matches a sequence against those in BLOCKS, PRINTS, DOMO, PRODOM, and PFAM databases to search for gene families, sequence homology, and structural fingerprint regions.	Henikoff, S and J.G. Henikoff, Nucl. Acid Res., 19:6565-72, 1991. J.G. Henikoff and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Attwood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37: 417-424.	Score=1000 or greater; Ratio of Score/Strength = 0.75 or larger; and, if applicable, Probability value= 1.0E-3 or less
HMMER	An algorithm for searching a query sequence against hidden Markov model (HMM)-based databases of protein family consensus sequences, such as PFAM.	Krogh, A. et al. (1994) J. Mol. Biol., 235:1501-1531; Sonnhammer, E.L.L. et al. (1988) Nucleic Acids Res. 26:320-322.	Score=10-50 bits for PFAM hits, depending on individual protein families

Table 5 cont.

Program	Description	Reference	Parameter Threshold
ProfileScan	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribskov, M. et al. (1988) CABIOS 4:61-66; Gribskov, et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25: 217-221.	Score= 4.0 or greater
Phred	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap	A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M. S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Score= 120 or greater; Match length= 56 or greater
Consed	A graphical tool for viewing and editing Phrap assemblies	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan	A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12: 431-439.	Score=5 or greater
Motif's	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch et al. <u>supra</u> ; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	

What is claimed is:

1. A substantially purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-65, and fragments thereof.
- 5 2. A substantially purified variant having at least 90% amino acid sequence identity to the amino acid sequence of claim 1.
3. An isolated and purified polynucleotide encoding the polypeptide of claim 1.
4. An isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide of claim 3.
- 10 5. An isolated and purified polynucleotide which hybridizes under stringent conditions to the polynucleotide of claim 3.
6. An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 3.
7. A method for detecting a polynucleotide, the method comprising the steps of:
  - 15 (a) hybridizing the polynucleotide of claim 6 to at least one nucleic acid in a sample, thereby forming a hybridization complex; and
  - (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of the polynucleotide in the sample.
8. The method of claim 7 further comprising amplifying the polynucleotide prior to  
20 hybridization.
9. An isolated and purified polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:66-130, and fragments thereof.
10. An isolated and purified polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide of claim 9.
- 25 11. An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 9.
12. An expression vector comprising at least a fragment of the polynucleotide of claim 3.
13. A host cell comprising the expression vector of claim 12.
- 30 14. A method for producing a polypeptide, the method comprising the steps of:
  - a) culturing the host cell of claim 13 under conditions suitable for the expression of the polypeptide; and
  - b) recovering the polypeptide from the host cell culture.
15. A pharmaceutical composition comprising the polypeptide of claim 1 in  
35 conjunction with a suitable pharmaceutical carrier.

16. A purified antibody which specifically binds to the polypeptide of claim 1.
17. A purified agonist of the polypeptide of claim 1.
18. A purified antagonist of the polypeptide of claim 1.
19. A method for treating or preventing a disorder associated with decreased  
5 expression or activity of HTRM, the method comprising administering to a subject in need of such treatment an effective amount of the pharmaceutical composition of claim 15.
20. A method for treating or preventing a disorder associated with increased expression or activity of HTRM, the method comprising administering to a subject in need of such treatment an effective amount of the antagonist of claim 18.

## SEQUENCE LISTING

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HILLMAN, Jennifer L.

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LAL, Preeti

YUE, Henry

REDDY, Roopa

TANG, Y. Tom

GERSTIN, Edward H.

PATTERSON, Chandra

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&lt;223&gt; Incyte clone 673766CD1

&lt;400&gt; 7

Met Glu Leu Glu	Leu Asp Ala Gly	Asp Gln Asp Leu Leu	Ala Phe
1	5	10	15
Leu Leu Glu Glu	Ser Gly Asp Leu Gly	Thr Ala Pro Asp Glu	Ala
	20	25	30
Val Arg Ala Pro	Leu Asp Trp Ala Leu	Pro Leu Ser Glu Val	Pro
	35	40	45
Ser Asp Trp Glu	Val Asp Asp Leu Leu	Cys Ser Leu Leu Ser	Pro
	50	55	60
Pro Ala Ser Leu	Asn Ile Leu Ser Ser	Ser Asn Pro Cys Leu	Val
	65	70	75
His His Asp His	Thr Tyr Ser Leu Pro	Arg Glu Thr Val Ser	Met
	80	85	90
Asp Leu Glu Ser	Glu Ser Cys Arg Lys	Glu Gly Thr Gln Met	Thr
	95	100	105
Pro Gln His Met	Glu Glu Leu Ala Glu	Gln Glu Ile Ala Arg	Leu
	110	115	120
Val Leu Thr Asp	Glu Glu Lys Ser Leu	Leu Glu Lys Glu Gly	Leu

Ile Leu Pro Glu	Thr Leu Pro Leu Thr	Lys Thr Glu Glu Gln	Ile
125	130	135	
Leu Lys Arg Val	Arg Arg Lys Ile Arg	Asn Lys Arg Ser Ala	Gln
140	145	150	
Glu Ser Arg Arg	Lys Lys Lys Val Tyr	Val Gly Gly Leu Glu	Ser
155	160	165	
Arg Val Leu Lys	Tyr Thr Ala Gln Asn	Met Glu Leu Gln Asn	Lys
170	175	180	
Val Gln Leu Leu	Glu Glu Gln Asn Leu	Ser Leu Leu Asp Gln	Leu
185	190	195	
Arg Lys Leu Gln	Ala Met Val Ile Glu	Ile Ser Asn Lys Thr	Ser
200	205	210	
Ser Ser Ser Thr	Cys Ile Leu Val Leu	Leu Val Ser Phe Cys	Leu
215	220	225	
Leu Leu Val Pro	Ala Met Tyr Ser Ser	Asp Thr Arg Gly Ser	Leu
230	235	240	
Pro Ala Glu His	Gly Val Leu Ser Arg	Gln Leu Arg Ala Leu	Pro
245	250	255	
Ser Glu Asp Pro	Tyr Gln Leu Glu Leu	Pro Ala Leu Gln Ser	Glu
260	265	270	
Val Pro Lys Asp	Ser Thr His Gln Trp	Leu Asp Gly Ser Asp	Cys
275	280	285	
Val Leu Gln Ala	Pro Gly Asn Thr Ser	Cys Leu Leu His Tyr	Met
290	295	300	
Pro Gln Ala Pro	Ser Ala Glu Pro Pro	Leu Glu Trp Pro Phe	Pro
305	310	315	
Asp Leu Phe Ser	Glu Pro Leu Cys Arg	Gly Pro Ile Leu Pro	Leu
320	325	330	
Gln Ala Asn Leu	Thr Arg Lys Gly Gly	Trp Leu Pro Thr Gly	Ser
335	340	345	
Pro Ser Val Ile	Leu Gln Asp Arg Tyr	Ser Gly	
350	355	360	
365	370		

&lt;210&gt; 8

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1504753CD1

&lt;400&gt; 8

Met Asn Ser Leu Ala Thr Ser Val Phe Ser	Ile Ala Ile Pro Val
1	5
Asp Gly Asp Glu Asp Arg Asn Pro Ser Thr	Ala Phe Tyr Gln Ala
20	25
Phe His Leu Asn Thr Leu Lys Glu Ser Lys	Ser Leu Trp Asp Ser
35	40
Ala Ser Gly Gly Gly Val Val Ala Ile Asp	Asn Lys Ile Glu Gln
50	55
Ala Met Asp Leu Val Lys Ser His Leu Met Tyr	Ala Val Arg Glu
65	70
Glu Val Glu Val Leu Lys Glu Gln Ile Lys	Glu Leu Val Glu Arg
80	85
Asn Ser Leu Leu Glu Arg Glu Asn Ala Leu	Leu Lys Ser Leu Ser
95	100
Ser Asn Asp Gln Leu Ser Gln Leu Pro Thr	Gln Gln Ala Asn Pro
110	115
Gly Ser Thr Ser Gln Gln Gln Ala Val Ile	Ala Gln Pro Pro Gln

		125						130				135
Pro	Thr	Gln	Pro	Pro	Gln	Gln	Pro	Asn	Val	Ser	Ser	Ala
				140					145			

<210> 9  
 <211> 127  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1760185CD1

<400> 9  
 Met Arg Pro Leu Asp Ile Val Glu Leu Ala Glu Pro Glu Glu Val  
   1                  5                  10                  15  
 Glu Val Leu Glu Pro Glu Glu Asp Phe Glu Gln Phe Leu Leu Pro  
                   20                  25                  30  
 Val Ile Asn Glu Met Arg Glu Asp Ile Ala Ser Leu Thr Arg Glu  
                   35                  40                  45  
 His Gly Arg Ala Tyr Leu Arg Asn Arg Ser Lys Leu Trp Glu Met  
                   50                  55                  60  
 Asp Asn Met Leu Ile Gln Ile Lys Thr Gln Val Glu Ala Ser Glu  
                   65                  70                  75  
 Glu Ser Ala Leu Asn His Leu Gln Asn Pro Gly Asp Ala Ala Glu  
                   80                  85                  90  
 Gly Arg Ala Ala Lys Arg Cys Glu Lys Ala Glu Glu Lys Ala Lys  
                   95                  100                 105  
 Glu Ile Ala Lys Met Ala Glu Met Leu Val Glu Leu Val Arg Arg  
                  110                 115                 120  
 Ile Glu Lys Ser Glu Ser Ser  
                  125

<210> 10  
 <211> 383  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1805061CD1

<400> 10  
 Met Pro Tyr Val Asp Arg Gln Asn Arg Ile Cys Gly Phe Leu Asp  
   1                  5                  10                 15  
 Ile Glu Glu Asn Glu Asn Ser Gly Lys Phe Leu Arg Arg Tyr Phe  
                   20                  25                  30  
 Ile Leu Asp Thr Arg Glu Asp Ser Phe Val Trp Tyr Met Asp Asn  
                   35                  40                  45  
 Pro Gln Asn Leu Pro Ser Gly Ser Ser Arg Val Gly Ala Ile Lys  
                   50                  55                  60  
 Leu Thr Tyr Ile Ser Lys Val Ser Asp Ala Thr Lys Leu Arg Pro  
                   65                  70                  75  
 Lys Ala Glu Phe Cys Phe Val Met Asn Ala Gly Met Arg Lys Tyr  
                   80                  85                  90  
 Phe Leu Gln Ala Asn Asp Gln Gln Asp Leu Val Glu Trp Val Asn  
                   95                 100                 105

Val	Leu	Asn	Lys	Ala 110	Ile	Lys	Ile	Thr	Val 115	Pro	Lys	Gln	Ser	Asp 120
Ser	Gln	Pro	Asn	Ser 125	Asp	Asn	Leu	Ser	Arg 130	His	Gly	Glu	Cys	Gly 135
Lys	Lys	Gln	Val	Ser 140	Tyr	Arg	Thr	Asp	Ile 145	Val	Gly	Gly	Val	Pro 150
Ile	Ile	Thr	Pro	Thr 155	Gln	Lys	Glu	Glu	Val 160	Asn	Glu	Cys	Gly	Glu 165
Ser	Ile	Asp	Arg	Asn 170	Asn	Leu	Lys	Arg	Ser 175	Gln	Ser	His	Leu	Pro 180
Tyr	Phe	Thr	Pro	Lys 185	Pro	Pro	Gln	Asp	Ser 190	Ala	Val	Ile	Lys	Ala 195
Gly	Tyr	Cys	Val	Lys 200	Gln	Gly	Ala	Val	Met 205	Lys	Asn	Trp	Lys	Arg 210
Arg	Tyr	Phe	Gln	Leu 215	Asp	Glu	Asn	Thr	Ile 220	Gly	Tyr	Phe	Lys	Ser 225
Glu	Leu	Glu	Lys	Glu 230	Pro	Leu	Arg	Val	Ile 235	Pro	Leu	Lys	Glu	Val 240
His	Lys	Val	Gln	Glu 245	Cys	Lys	Gln	Ser	Asp 250	Ile	Met	Met	Arg	Asp 255
Asn	Leu	Phe	Glu	Ile 260	Val	Thr	Thr	Ser	Arg 265	Thr	Phe	Tyr	Val	Gln 270
Ala	Asp	Ser	Pro	Glu 275	Glu	Met	His	Ser	Trp 280	Ile	Lys	Ala	Val	Ser 285
Gly	Ala	Ile	Val	Ala 290	Gln	Arg	Gly	Pro	Gly 295	Arg	Ser	Ala	Ser	Ser 300
Met	Arg	Gln	Ala	Arg 305	Arg	Leu	Ser	Asn	Pro 310	Cys	Ile	Gln	Arg	Ser 315
Ile	Pro	Pro	Val	Leu 320	Gln	Asn	Pro	Asn	Thr 325	Leu	Ser	Val	Leu	Pro 330
Thr	Gln	Pro	Pro	Pro 335	Pro	His	Ile	Pro	Gln 340	Pro	Leu	Ala	Ala	Thr 345
Leu	Trp	Ser	Gln	Pro 350	Leu	Pro	Trp	Arg	Ser 355	Glu	Asp	Phe	Thr	Ser 360
Leu	Leu	Pro	Arg	Ser 365	Ser	Gln	Gly	Thr	Ser 370	Arg	Ser	Arg	Leu	Ser 375
Leu	Gln	Glu	Asn	Gln 380	Leu	Pro	Lys							

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<210> 11
<211> 254
<212> PRT
<213> Homo sapiens
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<220>  
<221> misc_feature  
<223> Incyte clone 1850120CD1
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<400> 11														
Met	Ser	Leu	Ala	Arg	Gly	His	Gly	Asp	Thr	Ala	Ala	Ser	Thr	Ala
1				5					10					15
Ala	Pro	Leu	Ser	Glu	Glu	Gly	Glu	Val	Thr	Ser	Gly	Leu	Gln	Ala
				20					25					30
Leu	Ala	Val	Glu	Asp	Thr	Gly	Gly	Pro	Ser	Ala	Ser	Ala	Gly	Lys
				35					40					45
Ala	Glu	Asp	Glu	Gly	Glu	Gly	Gly	Arg	Glu	Glu	Thr	Glu	Arg	Glu
				50					55					60
Gly	Ser	Gly	Gly	Glu	Glu	Ala	Gln	Gly	Glu	Val	Pro	Ser	Ala	Gly
				65					70					75
Gly	Glu	Glu	Pro	Ala	Glu	Glu	Asp	Ser	Glu	Asp	Trp	Cys	Val	Pro
				80					85					90
Cys	Ser	Asp	Glu	Glu	Val	Glu	Leu	Pro	Ala	Asp	Gly	Gln	Pro	Trp
				95					100					105

Met	Pro	Pro	Pro	Ser	Glu	Ile	Gln	Arg	Leu	Tyr	Glu	Leu	Leu	Ala
				110					115					120
Ala	His	Gly	Thr	Leu	Glu	Leu	Gln	Ala	Glu	Ile	Leu	Pro	Arg	Arg
				125					130					135
Pro	Pro	Thr	Pro	Glu	Arg	Gln	Ser	Glu	Glu	Glu	Arg	Ser	Asp	Glu
				140					145					150
Glu	Pro	Glu	Ala	Lys	Glu	Glu	Glu	Glu	Glu	Lys	Pro	His	Met	Pro
				155					160					165
Thr	Glu	Phe	Asp	Phe	Asp	Asp	Glu	Pro	Val	Thr	Pro	Lys	Asp	Ser
				170					175					180
Leu	Ile	Asp	Arg	Arg	Arg	Thr	Pro	Gly	Ser	Ser	Ala	Arg	Ser	Gln
				185					190					195
Lys	Arg	Glu	Ala	Arg	Leu	Asp	Lys	Val	Leu	Ser	Asp	Met	Lys	Arg
				200					205					210
His	Lys	Lys	Leu	Glu	Glu	Gln	Ile	Leu	Arg	Thr	Gly	Arg	Asp	Leu
				215					220					225
Phe	Ser	Leu	Asp	Ser	Glu	Asp	Pro	Ser	Pro	Ala	Ser	Pro	Pro	Leu
				230					235					240
Arg	Ser	Ser	Gly	Ser	Ser	Leu	Phe	Pro	Arg	Gln	Arg	Lys	Tyr	
				245					250					

&lt;210&gt; 12

&lt;211&gt; 305

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1852290CD1

&lt;400&gt; 12

Met	Ala	Leu	Cys	Ala	Leu	Thr	Arg	Ala	Leu	Arg	Ser	Leu	Asn	Leu
1				5					10					15
Ala	Pro	Pro	Thr	Val	Ala	Ala	Pro	Ala	Pro	Ser	Leu	Phe	Pro	Ala
				20					25					30
Ala	Gln	Met	Met	Asn	Asn	Gly	Leu	Leu	Gln	Gln	Pro	Ser	Ala	Leu
				35					40					45
Met	Leu	Leu	Pro	Cys	Arg	Pro	Val	Leu	Thr	Ser	Val	Ala	Leu	Asn
				50					55					60
Ala	Asn	Phe	Val	Ser	Trp	Lys	Ser	Arg	Thr	Lys	Tyr	Thr	Ile	Thr
				65					70					75
Pro	Val	Lys	Met	Arg	Lys	Ser	Gly	Gly	Arg	Asp	His	Thr	Gly	Arg
				80					85					90
Ile	Arg	Val	His	Gly	Ile	Gly	Gly	Gly	His	Lys	Gln	Arg	Tyr	Arg
				95					100					105
Met	Ile	Asp	Phe	Leu	Arg	Phe	Arg	Pro	Glu	Glu	Thr	Lys	Ser	Gly
				110					115					120
Pro	Phe	Glu	Glu	Lys	Val	Ile	Gln	Val	Arg	Tyr	Asp	Pro	Cys	Arg
				125					130					135
Ser	Ala	Asp	Ile	Ala	Leu	Val	Ala	Gly	Gly	Ser	Arg	Lys	Arg	Trp
				140					145					150
Ile	Ile	Ala	Thr	Glu	Asn	Met	Gln	Ala	Gly	Asp	Thr	Ile	Leu	Asn
				155					160					165
Ser	Asn	His	Ile	Gly	Arg	Met	Ala	Val	Ala	Ala	Arg	Glu	Gly	Asp
				170					175					180
Ala	His	Pro	Leu	Gly	Ala	Leu	Pro	Val	Gly	Thr	Leu	Ile	Asn	Asn
				185					190					195
Val	Glu	Ser	Glu	Pro	Gly	Arg	Gly	Ala	Gln	Tyr	Ile	Arg	Ala	Ala
				200					205					210
Gly	Thr	Cys	Gly	Val	Leu	Leu	Arg	Lys	Val	Asn	Gly	Thr	Ala	Ile
				215					220					225

Ile	Gln	Leu	Pro	Ser	Lys	Arg	Gln	Met	Gln	Val	Leu	Glu	Thr	Cys	
				230					235					240	
Val	Ala	Thr	Val	Gly	Arg	Val	Ser	Asn	Val	Asp	His	Asn	Lys	Arg	
				245					250					255	
Val	Ile	Gly	Lys	Ala	Gly	Arg	Asn	Arg	Trp	Leu	Gly	Lys	Arg	Pro	
				260					265					270	
Asn	Ser	Gly	Arg	Trp	His	Arg	Lys	Gly	Gly	Trp	Ala	Gly	Arg	Lys	
				275					280					285	
Ile	Arg	Pro	Leu	Pro	Pro	Met	Lys	Ser	Tyr	Val	Lys	Leu	Pro	Ser	
				290					295					300	
Ala	Ser	Ala	Gln	Ser											
				305											

&lt;210&gt; 13

&lt;211&gt; 230

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1944530CD1

&lt;400&gt; 13

Met	Gly	Gln	Gln	Ile	Ser	Asp	Gln	Thr	Gln	Leu	Val	Ile	Asn	Lys	
1				5					10					15	
Leu	Pro	Glu	Lys	Val	Ala	Lys	His	Val	Thr	Leu	Val	Arg	Glu	Ser	
				20					25					30	
Gly	Ser	Leu	Thr	Tyr	Glu	Glu	Phe	Leu	Gly	Arg	Val	Ala	Glu	Leu	
				35					40					45	
Asn	Asp	Val	Thr	Ala	Lys	Val	Ala	Ser	Gly	Gln	Glu	Lys	His	Leu	
				50					55					60	
Leu	Phe	Glu	Val	Gln	Pro	Gly	Ser	Asp	Ser	Ser	Ala	Phe	Trp	Lys	
				65					70					75	
Val	Val	Val	Arg	Val	Val	Cys	Thr	Lys	Ile	Asn	Lys	Ser	Ser	Gly	
				80					85					90	
Ile	Val	Glu	Ala	Ser	Arg	Ile	Met	Asn	Leu	Tyr	Gln	Phe	Ile	Gln	
				95					100					105	
Leu	Tyr	Lys	Asp	Ile	Thr	Ser	Gln	Ala	Ala	Gly	Val	Leu	Ala	Gln	
				110					115					120	
Ser	Ser	Thr	Ser	Glu	Glu	Pro	Asp	Glu	Asn	Ser	Ser	Ser	Val	Thr	
				125					130					135	
Ser	Cys	Gln	Ala	Ser	Leu	Trp	Met	Gly	Arg	Val	Lys	Gln	Leu	Thr	
				140					145					150	
Asp	Glu	Glu	Glu	Cys	Cys	Ile	Cys	Met	Asp	Gly	Arg	Ala	Asp	Leu	
				155					160					165	
Ile	Leu	Pro	Cys	Ala	His	Ser	Phe	Cys	Gln	Lys	Cys	Ile	Asp	Lys	
				170					175					180	
Trp	Ser	Asp	Arg	His	Arg	Asn	Cys	Pro	Ile	Cys	Arg	Leu	Gln	Met	
				185					190					195	
Thr	Gly	Ala	Asn	Glu	Ser	Trp	Val	Val	Ser	Asp	Ala	Pro	Thr	Glu	
				200					205					210	
Asp	Asp	Met	Ala	Asn	Tyr	Ile	Leu	Asn	Met	Ala	Asp	Glu	Ala	Gly	
				215					220					225	
Gln	Pro	His	Arg	Pro											
				230											

&lt;210&gt; 14

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;



&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2019742CB1

&lt;400&gt; 14

```

Met Ser Gly Met Glu Ala Thr Val Thr Ile Pro Ile Trp Gln Asn
 1          5          10          15
Lys Pro His Gly Ala Ala Arg Ser Val Val Arg Arg Ile Gly Thr
          20          25          30
Asn Leu Pro Leu Lys Pro Cys Ala Arg Ala Ser Phe Glu Thr Leu
          35          40          45
Pro Asn Ile Ser Asp Leu Cys Leu Arg Asp Val Pro Pro Val Pro
          50          55          60
Thr Leu Ala Asp Ile Ala Trp Ile Ala Ala Asp Glu Glu Glu Thr
          65          70          75
Tyr Ala Arg Val Arg Ser Asp Thr Arg Pro Leu Arg His Thr Trp
          80          85          90
Lys Pro Ser Pro Leu Ile Val Met Gln Arg Asn Ala Ser Val Pro
          95          100          105
Asn Leu Arg Gly Ser Glu Glu Arg Leu Leu Ala Leu Lys Lys Pro
          110          115          120
Ala Leu Pro Ala Leu Ser Arg Thr Thr Glu Leu Gln Asp Glu Leu
          125          130          135
Ser His Leu Arg Ser Gln Ile Ala Lys Ile Val Ala Ala Asp Ala
          140          145          150
Ala Ser Ala Ser Leu Thr Pro Asp Phe Leu Ser Pro Gly Ser Ser
          155          160          165
Asn Val Ser Ser Pro Leu Pro Cys Phe Gly Ser Ser Phe His Ser
          170          175          180
Thr Thr Ser Phe Val Ile Ser Asp Ile Thr Glu Glu Thr Glu Val
          185          190          195
Glu Val Pro Glu Leu Pro Ser Val Pro Leu Leu Cys Ser Ala Ser
          200          205          210
Pro Glu Cys Cys Lys Pro Glu His Lys Ala Ala Cys Ser Ser Ser
          215          220          225
Glu Glu Asp Asp Cys Val Ser Leu Ser Lys Ala Ser Ser Phe Ala
          230          235          240
Asp Met Met Gly Ile Leu Lys Asp Phe His Arg Met Lys Gln Ser
          245          250          255
Gln Asp Leu Asn Arg Ser Leu Leu Lys Glu Glu Asp Pro Ala Val
          260          265          270
Leu Ile Ser Glu Val Leu Arg Arg Lys Phe Ala Leu Lys Glu Glu
          275          280          285
Asp Ile Ser Arg Lys Gly Asn
          290

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&lt;210&gt; 15

&lt;211&gt; 232

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2056042CD1

&lt;400&gt; 15

```

Met Ala Ser Ser Ala Ala Ser Ser Glu His Phe Glu Lys Leu His
 1          5          10          15
Glu Ile Phe Arg Gly Leu His Glu Asp Leu Gln Gly Val Pro Glu
          20          25          30
Arg Leu Leu Gly Thr Ala Gly Thr Glu Glu Lys Lys Lys Leu Ile
          35          40          45
Arg Asp Phe Asp Glu Lys Gln Gln Glu Ala Asn Glu Thr Leu Ala
          50          55          60

```

Glu	Met	Glu	Glu	Glu	Leu	Arg	Tyr	Ala	Pro	Leu	Ser	Phe	Arg	Asn	
				65					70					75	
Pro	Met	Met	Ser	Lys	Leu	Arg	Asn	Tyr	Arg	Lys	Asp	Leu	Ala	Lys	
				80					85					90	
Leu	His	Arg	Glu	Val	Arg	Ser	Thr	Pro	Leu	Thr	Ala	Thr	Pro	Gly	
				95					100					105	
Gly	Arg	Gly	Asp	Met	Lys	Tyr	Gly	Ile	Tyr	Ala	Val	Glu	Asn	Glu	
				110					115					120	
His	Met	Asn	Arg	Leu	Gln	Ser	Gln	Arg	Ala	Met	Leu	Leu	Gln	Gly	
				125					130					135	
Thr	Glu	Ser	Leu	Asn	Arg	Ala	Thr	Gln	Ser	Ile	Glu	Arg	Ser	His	
				140					145					150	
Arg	Ile	Ala	Thr	Glu	Thr	Asp	Gln	Ile	Gly	Ser	Glu	Ile	Ile	Glu	
				155					160					165	
Glu	Leu	Gly	Glu	Gln	Arg	Asp	Gln	Leu	Glu	Arg	Thr	Lys	Ser	Arg	
				170					175					180	
Leu	Val	Asn	Thr	Ser	Glu	Asn	Leu	Ser	Lys	Ser	Arg	Lys	Ile	Leu	
				185					190					195	
Arg	Ser	Met	Ser	Arg	Lys	Val	Thr	Thr	Asn	Lys	Leu	Leu	Leu	Ser	
				200					205					210	
Ile	Ile	Ile	Leu	Leu	Glu	Leu	Ala	Ile	Leu	Gly	Gly	Leu	Val	Tyr	
				215					220					225	
Tyr	Lys	Phe	Phe	Arg	Ser	His									
				230											

&lt;210&gt; 16

&lt;211&gt; 376

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;223&gt; Incyte clone 2398682CD1

&lt;400&gt; 16

Met	Arg	Gly	Lys	Thr	Phe	Arg	Phe	Glu	Met	Gln	Arg	Asp	Leu	Val	
1				5					10					15	
Ser	Phe	Pro	Leu	Ser	Pro	Ala	Val	Arg	Val	Lys	Leu	Val	Ser	Ala	
				20					25					30	
Gly	Phe	Gln	Thr	Ala	Glu	Glu	Leu	Leu	Glu	Val	Lys	Pro	Ser	Glu	
				35					40					45	
Leu	Ser	Lys	Glu	Val	Gly	Ile	Ser	Lys	Ala	Glu	Ala	Leu	Glu	Thr	
				50					55					60	
Leu	Gln	Ile	Ile	Arg	Arg	Glu	Cys	Leu	Thr	Asn	Lys	Pro	Arg	Tyr	
				65					70					75	
Ala	Gly	Thr	Ser	Glu	Ser	His	Lys	Lys	Cys	Thr	Ala	Leu	Glu	Leu	
				80					85					90	
Leu	Glu	Gln	Glu	His	Thr	Gln	Gly	Phe	Ile	Ile	Thr	Phe	Cys	Ser	
				95					100					105	
Ala	Leu	Asp	Asp	Ile	Leu	Gly	Gly	Gly	Val	Pro	Leu	Met	Lys	Thr	
				110					115					120	
Thr	Glu	Ile	Cys	Gly	Ala	Pro	Gly	Val	Gly	Lys	Thr	Gln	Leu	Cys	
				125					130					135	
Met	Gln	Leu	Ala	Val	Asp	Val	Gln	Ile	Pro	Glu	Cys	Phe	Gly	Gly	
				140					145					150	
Val	Ala	Gly	Glu	Ala	Val	Phe	Ile	Asp	Thr	Glu	Gly	Ser	Phe	Met	
				155					160					165	
Val	Asp	Arg	Val	Val	Asp	Leu	Ala	Thr	Ala	Cys	Ile	Gln	His	Leu	
				170					175					180	
Gln	Leu	Ile	Ala	Glu	Lys	His	Lys	Gly	Glu	Glu	His	Arg	Lys	Ala	
				185					190					195	

Leu	Glu	Asp	Phe	Thr	Leu	Asp	Asn	Ile	Leu	Ser	His	Ile	Tyr	Tyr	
				200						205					210
Phe	Arg	Cys	Arg	Asp	Tyr	Thr	Glu	Leu	Leu	Ala	Gln	Val	Tyr	Leu	
				215						220					225
Leu	Pro	Asp	Phe	Leu	Ser	Glu	His	Ser	Lys	Val	Arg	Leu	Val	Ile	
				230						235					240
Val	Asp	Gly	Ile	Ala	Phe	Pro	Phe	Arg	His	Asp	Leu	Asp	Asp	Leu	
				245						250					255
Ser	Leu	Arg	Thr	Arg	Leu	Leu	Asn	Gly	Leu	Ala	Gln	Gln	Met	Ile	
				260						265					270
Ser	Leu	Ala	Asn	Asn	His	Arg	Leu	Ala	Val	Ile	Leu	Thr	Asn	Gln	
				275						280					285
Met	Thr	Thr	Lys	Ile	Asp	Arg	Asn	Gln	Ala	Leu	Leu	Val	Pro	Ala	
				290						295					300
Leu	Gly	Glu	Ser	Trp	Gly	His	Ala	Ala	Thr	Ile	Arg	Leu	Ile	Phe	
				305						310					315
His	Trp	Asp	Arg	Lys	Gln	Arg	Leu	Ala	Thr	Leu	Tyr	Lys	Ser	Pro	
				320						325					330
Ser	Gln	Lys	Glu	Cys	Thr	Val	Leu	Phe	Gln	Ile	Lys	Pro	Gln	Gly	
				335						340					345
Phe	Arg	Asp	Thr	Val	Val	Thr	Ser	Ala	Cys	Ser	Leu	Gln	Thr	Glu	
				350						355					360
Gly	Ser	Leu	Ser	Thr	Arg	Lys	Arg	Ser	Arg	Asp	Pro	Glu	Glu	Glu	
				365						370					375

Leu

&lt;210&gt; 17

&lt;211&gt; 204

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2518753CD1

&lt;400&gt; 17

Met	Ala	Lys	Val	Gln	Val	Asn	Asn	Val	Val	Val	Leu	Asp	Asn	Pro	
1				5						10				15	
Ser	Pro	Phe	Tyr	Asn	Pro	Phe	Gln	Phe	Glu	Ile	Thr	Phe	Glu	Cys	
				20						25				30	
Ile	Glu	Asp	Leu	Ser	Glu	Asp	Leu	Glu	Trp	Lys	Ile	Ile	Tyr	Val	
				35						40				45	
Gly	Ser	Ala	Glu	Ser	Glu	Glu	Tyr	Asp	Gln	Val	Leu	Asp	Ser	Val	
				50						55				60	
Leu	Val	Gly	Pro	Val	Pro	Ala	Gly	Arg	His	Met	Phe	Val	Phe	Gln	
				65						70				75	
Ala	Asp	Ala	Pro	Asn	Pro	Gly	Leu	Ile	Pro	Asp	Ala	Asp	Ala	Val	
				80						85				90	
Gly	Val	Thr	Val	Val	Leu	Ile	Thr	Cys	Thr	Tyr	Arg	Gly	Gln	Glu	
				95						100				105	
Phe	Ile	Arg	Val	Gly	Tyr	Tyr	Val	Asn	Asn	Glu	Tyr	Thr	Glu	Thr	
				110						115				120	
Glu	Leu	Arg	Glu	Asn	Pro	Pro	Val	Lys	Pro	Asp	Phe	Ser	Lys	Leu	
				125						130				135	
Gln	Arg	Asn	Ile	Leu	Ala	Ser	Asn	Pro	Arg	Val	Thr	Arg	Phe	His	
				140						145				150	
Ile	Asn	Trp	Glu	Asp	Asn	Thr	Glu	Lys	Leu	Glu	Asp	Ala	Glu	Ser	
				155						160				165	
Ser	Asn	Pro	Asn	Leu	Gln	Ser	Leu	Leu	Ser	Thr	Asp	Ala	Leu	Pro	
				170						175				180	
Ser	Ala	Ser	Lys	Gly	Trp	Ser	Thr	Ser	Glu	Asn	Ser	Leu	Asn	Val	
				185						190				195	

Met Leu Glu Ser His Met Asp Cys Met

200

<210> 18  
 <211> 713  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 2709055CD1

<400> 18

Met	Tyr	Leu	Leu	Ile	Gln	Met	Cys	Tyr	His	Leu	Ala	Leu	Pro	Trp	
1				5					10					15	
Tyr	Ser	Lys	Tyr	Phe	Pro	Tyr	Leu	Ala	Leu	Ile	His	Thr	Ile	Ile	
				20					25					30	
Leu	Met	Ala	Ser	Ser	Asn	Phe	Trp	Phe	Lys	Tyr	Pro	Lys	Thr	Cys	
				35					40					45	
Ser	Lys	Val	Glu	His	Ser	Val	Ser	Ile	Leu	Gly	Lys	Cys	Phe	Glu	
				50					55					60	
Ser	Pro	Trp	Thr	Thr	Lys	Ala	Leu	Ser	Glu	Thr	Ala	Cys	Glu	Asp	
				65					70					75	
Ser	Glu	Glu	Asn	Lys	Gln	Arg	Ile	Thr	Gly	Ala	Gln	Thr	Leu	Pro	
				80					85					90	
Lys	His	Val	Ser	Thr	Ser	Ser	Asp	Glu	Gly	Ser	Pro	Ser	Ala	Ser	
				95					100					105	
Thr	Pro	Met	Ile	Asn	Lys	Thr	Gly	Phe	Lys	Phe	Ser	Ala	Glu	Lys	
				110					115					120	
Pro	Val	Ile	Glu	Val	Pro	Ser	Met	Thr	Ile	Leu	Asp	Lys	Lys	Asp	
				125					130					135	
Gly	Glu	Gln	Ala	Lys	Ala	Leu	Phe	Glu	Lys	Val	Arg	Lys	Phe	Arg	
				140					145					150	
Ala	His	Val	Glu	Asp	Ser	Asp	Leu	Ile	Tyr	Lys	Leu	Tyr	Val	Val	
				155					160					165	
Gln	Thr	Val	Ile	Lys	Thr	Ala	Lys	Phe	Ile	Phe	Ile	Leu	Cys	Tyr	
				170					175					180	
Thr	Ala	Asn	Phe	Val	Asn	Ala	Ile	Ser	Phe	Glu	His	Val	Cys	Lys	
				185					190					195	
Pro	Lys	Val	Glu	His	Leu	Ile	Gly	Tyr	Glu	Val	Phe	Glu	Cys	Thr	
				200					205					210	
His	Asn	Met	Ala	Tyr	Met	Leu	Lys	Lys	Leu	Leu	Ile	Ser	Tyr	Ile	
				215					220					225	
Ser	Ile	Ile	Cys	Val	Tyr	Gly	Phe	Ile	Cys	Leu	Tyr	Thr	Leu	Phe	
				230					235					240	
Trp	Leu	Phe	Arg	Ile	Pro	Leu	Lys	Glu	Tyr	Ser	Phe	Glu	Lys	Val	
				245					250					255	
Arg	Glu	Glu	Ser	Ser	Phe	Ser	Asp	Ile	Pro	Asp	Val	Lys	Asn	Asp	
				260					265					270	
Phe	Ala	Phe	Leu	Leu	His	Met	Val	Asp	Gln	Tyr	Asp	Gln	Leu	Tyr	
				275					280					285	
Ser	Lys	Arg	Phe	Gly	Val	Phe	Leu	Ser	Glu	Val	Ser	Glu	Asn	Lys	
				290					295					300	
Leu	Arg	Glu	Ile	Ser	Leu	Asn	His	Glu	Trp	Thr	Phe	Glu	Lys	Leu	
				305					310					315	
Arg	Gln	His	Ile	Ser	Arg	Asn	Ala	Gln	Asp	Lys	Gln	Glu	Leu	His	
				320					325					330	
Leu	Phe	Met	Leu	Ser	Gly	Val	Pro	Asp	Ala	Val	Phe	Asp	Leu	Thr	
				335					340					345	
Asp	Leu	Asp	Val	Leu	Lys	Leu	Glu	Leu	Ile	Pro	Glu	Ala	Lys	Ile	
				350					355					360	
Pro	Ala	Lys	Ile	Ser	Gln	Met	Thr	Asn	Leu	Gln	Glu	Leu	His	Leu	
				365					370					375	
Cys	His	Cys	Pro	Ala	Lys	Val	Glu	Gln	Thr	Ala	Phe	Ser	Phe	Leu	

Arg Asp His Leu	380	Arg Cys Leu His Val	385	Lys Phe Thr Asp Val	390
Glu Ile Pro Ala	395	Trp Val Tyr Leu Leu	400	Lys Asn Leu Arg Glu	405
Tyr Leu Ile Gly	410	Asn Leu Asn Ser Glu	415	Asn Asn Lys Met Ile	420
Leu Glu Ser Leu	425	Arg Glu Leu Arg His	430	Leu Lys Ile Leu His	435
Lys Ser Asn Leu	440	Thr Lys Val Pro Ser	445	Asn Ile Thr Asp Val	450
Pro His Leu Thr	455	Lys Leu Val Ile His	460	Asn Asp Gly Thr Lys	465
Leu Val Leu Asn	470	Ser Leu Lys Lys Met	475	Met Asn Val Ala Glu	480
Glu Leu Gln Asn	485	Cys Glu Leu Glu Arg	490	Ile Pro His Ala Ile	495
Ser Leu Ser Asn	500	Leu Gln Glu Leu Asp	505	Leu Lys Ser Asn Asn	510
Arg Thr Ile Glu	515	Glu Ile Ile Ser Phe	520	Gln His Leu Lys Arg	525
Thr Cys Leu Lys	530	Leu Trp His Asn Lys	535	Ile Val Thr Ile Pro	540
Ser Ile Thr His	545	Val Lys Asn Leu Glu	550	Ser Leu Tyr Phe Ser	555
Asn Lys Leu Glu	560	Ser Leu Pro Val Ala	565	Val Phe Ser Leu Gln	570
Leu Arg Cys Leu	575	Asp Val Ser Tyr Asn	580	Asn Ile Ser Met Ile	585
Ile Glu Ile Gly	590	Leu Leu Gln Asn Leu	595	Gln His Leu His Ile	600
Gly Asn Lys Val	605	Asp Ile Leu Pro Lys	610	Gln Leu Phe Lys Cys	615
Lys Leu Arg Thr	620	Leu Asn Leu Gly Gln	625	Asn Cys Ile Thr Ser	630
Pro Glu Lys Val	635	Gly Gln Leu Ser Gln	640	Leu Thr Gln Leu Glu	645
Lys Gly Asn Cys	650	Leu Asp Arg Leu Pro	655	Ala Gln Leu Gly Gln	660
Arg Met Leu Lys	665	Lys Ser Gly Leu Val	670	Val Glu Asp His Leu	675
Asp Thr Leu Pro	680	Leu Glu Val Lys Glu	685	Ala Leu Asn Gln Asp	690
Asn Ile Pro Phe	695	Ala Asn Gly Ile	700		705
	710				

&lt;210&gt; 19

&lt;211&gt; 360

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2724537CD1

&lt;400&gt; 19

Met Ala Ser Leu Leu Ala Lys Asp Ala Tyr Leu Gln Ser Leu Ala	1	5	10	15
Lys Lys Ile Cys Ser His Ser Ala Pro Glu Gln Gln Ala Arg Thr	20	25	30	
Arg Ala Gly Lys Thr Gln Gly Ser Glu Thr Ala Gly Pro Pro Lys	35	40	45	
Lys Lys Arg Lys Lys Thr Gln Lys Lys Phe Arg Lys Arg Glu Glu				

50	Lys Ala Ala Glu His	55	Lys Ala Lys Ser Leu Gly Glu Lys Ser Pro	60
65	Ala Ala Ser Gly Ala	70	Ala Ala Lys Glu Glu Ala	75
80	Ala Trp Ala Ser Ser	85	Pro Ala Asp Gly Leu Ala	90
95	Thr Glu Pro Glu Ser	100	Val Leu Arg Gln Arg	105
110	Leu His Glu Lys Ile	115	Gln Gly Ser Ala Lys	120
125	Glu Leu Ser Pro Ala	130	Arg Arg Arg Arg Lys Gln	135
140	Glu Arg Asp Arg Lys	145	Lys Glu Leu Arg Ala Lys	150
155	Glu Lys Ala Arg Lys	160	Thr Glu Ala Gln Glu Val	165
170	Val Glu Ala Thr Pro	175	Glu Pro Arg Glu Pro	180
185	Pro Gly Leu Ile Phe	190	Val Ser Glu Asp Glu Pro	195
200	Ala Ser Lys Ala Gln	205	Lys Arg Gln Arg Val Lys	210
215	Gly Asn Leu Thr Pro	220	Asn Tyr Arg Gln Leu Leu	225
230	Glu Arg Leu Gln Ala	235	Leu Asp Glu Leu Arg Gly	240
245	Gln Asp Glu Gly Lys	250	Glu Ala Lys Met Lys Trp	255
260	Thr Asn Leu Leu Tyr	265	Val Lys Ile Arg Asp Asp	270
275	Glu Arg Leu Leu Gln	280	Arg Lys Glu Lys Arg Arg	285
290	Ala Gln Arg Gln Arg	295	Thr Ala Gly Val Val	300
305	Glu Lys Met Gln Gln	310	Arg Arg Gln Asn Leu Arg	315
320	Arg Lys Lys Ala Ala	325	Leu Leu Arg Ala Arg	330
335	Lys Lys Gly Arg Ile	340	Leu Glu Arg Ala Gly Leu	345
350		355		360

&lt;210&gt; 20

&lt;211&gt; 196

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 025818CD1

&lt;400&gt; 20

Met Pro Ala Asp Ile	Met Glu Lys Asn Ser	Ser Ser Pro Val Ala
1	5	10
Ala Thr Pro Ala Ser	Val Asn Thr Thr Pro	Asp Lys Pro Lys Thr
20	25	30
Ala Ser Glu His Arg	Lys Ser Ser Lys Pro	Ile Met Glu Lys Arg
35	40	45
Arg Arg Ala Arg Ile	Asn Glu Ser Leu Ser	Gln Leu Lys Thr Leu
50	55	60
Ile Leu Asp Ala Leu	Lys Lys Asp Ser Ser	Arg His Ser Lys Leu

	65		70		75
Glu Lys Ala Asp Ile	Leu Glu Met Thr	Val Lys His Leu Arg Asn			
	80		85		90
Leu Gln Arg Ala Gln	Met Thr Ala Ala	Leu Ser Thr Asp Pro Ser			
	95		100		105
Val Leu Gly Lys Tyr	Arg Ala Gly Phe	Ser Glu Cys Met Asn Glu			
	110		115		120
Val Thr Arg Phe Leu	Ser Ser Pro Ser	Thr Pro Ala Thr Ala Ala			
	125		130		135
Pro Pro Trp Ala Pro	Thr Gln Cys His	Leu Pro Ala Ala Pro Arg			
	140		145		150
Leu Arg Arg Thr Pro	Cys Gly Gly Arg	Gly Gly Thr Glu Gly Ala			
	155		160		165
Gln Ala Thr Pro Pro	Pro Lys Leu Pro	Asn Pro Pro Leu Phe Pro			
	170		175		180
Pro Asp Ser Lys Gln	Glu Leu Glu Tyr	Trp Glu Arg Arg Gly Leu			
	185		190		195
Phe					

<210> 21  
 <211> 540  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 438283CD1

<400> 21

Met Leu Arg Glu Glu	Ala Thr Lys Lys Ser	Lys Glu Lys Glu Pro			
1	5	10			15
Gly Met Ala Leu Pro	Gln Gly Arg Leu Ala	Phe Arg Asp Val Ala			
	20	25			30
Ile Glu Phe Ser Leu	Glu Glu Trp Lys Cys	Leu Asn Pro Ala Gln			
	35	40			45
Arg Ala Leu Tyr Arg	Ala Val Met Leu Glu	Asn Tyr Arg Asn Leu			
	50	55			60
Glu Phe Val Asp Ser	Ser Leu Lys Ser Met	Met Glu Phe Ser Ser			
	65	70			75
Thr Arg His Ser Asn	Thr Gly Glu Val Ile	His Thr Gly Thr Leu			
	80	85			90
Gln Arg His Lys Ser	His His Ile Gly Asp	Phe Cys Phe Pro Glu			
	95	100			105
Met Lys Lys Asp Ile	His His Phe Glu Phe	Gln Trp Gln Glu Val			
	110	115			120
Glu Arg Asn Gly His	Glu Ala Pro Met Thr	Lys Ile Lys Lys Leu			
	125	130			135
Thr Gly Ser Thr Asp	Arg Ser Asp His Arg	His Ala Gly Asn Lys			
	140	145			150
Pro Ile Lys Asp Gln	Leu Gly Leu Ser Phe	His Ser His Leu Pro			
	155	160			165
Glu Leu His Met Phe	Gln Thr Lys Gly Lys	Ile Ser Asn Gln Leu			
	170	175			180
Asp Lys Ser Ile Ser	Gly Ala Ser Ser Ala	Ser Glu Ser Gln Arg			
	185	190			195
Ile Ser Cys Arg Leu	Lys Thr His Ile Ser	Asn Lys Tyr Gly Lys			
	200	205			210
Asn Phe Leu His Ser	Ser Phe Thr Gln Ile	Gln Glu Ile Cys Met			
	215	220			225
Arg Glu Lys Pro Cys	Gln Ser Asn Glu Cys	Gly Lys Ala Phe Asn			
	230	235			240

Tyr	Ser	Ser	Leu	Leu	Arg	Arg	His	His	Ile	Thr	His	Ser	Arg	Glu
				245					250					255
Arg	Glu	Tyr	Lys	Cys	Asp	Val	Cys	Gly	Lys	Ile	Phe	Asn	Gln	Lys
				260					265					270
Gln	Tyr	Ile	Val	Tyr	His	His	Arg	Cys	His	Thr	Gly	Glu	Lys	Thr
				275					280					285
Tyr	Lys	Cys	Asn	Glu	Cys	Gly	Lys	Thr	Phe	Thr	Gln	Met	Ser	Ser
				290					295					300
Leu	Val	Cys	His	Arg	Arg	Leu	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys
				305					310					315
Cys	Asn	Glu	Cys	Gly	Lys	Thr	Phe	Ser	Glu	Lys	Ser	Ser	Leu	Arg
				320					325					330
Cys	His	Arg	Arg	Leu	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Asn
				335					340					345
Glu	Cys	Gly	Lys	Thr	Phe	Gly	Arg	Asn	Ser	Ala	Leu	Val	Ile	His
				350					355					360
Lys	Ala	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Asn	Glu	Cys
				365					370					375
Gly	Lys	Thr	Phe	Ser	Gln	Lys	Ser	Ser	Leu	Gln	Cys	His	His	Ile
				380					385					390
Leu	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Glu	Glu	Cys	Asp	Asn
				395					400					405
Val	Tyr	Ile	Arg	Arg	Ser	His	Leu	Glu	Arg	His	Arg	Lys	Ile	His
				410					415					420
Thr	Gly	Glu	Gly	Ser	Tyr	Lys	Cys	Lys	Val	Cys	Asp	Lys	Ala	Phe
				425					430					435
Arg	Ser	Asp	Ser	Cys	Leu	Ala	Asn	His	Thr	Arg	Val	His	Thr	Gly
				440					445					450
Glu	Lys	Pro	Tyr	Lys	Cys	Asn	Lys	Cys	Ala	Lys	Val	Phe	Asn	Gln
				455					460					465
Lys	Gly	Ile	Leu	Ala	Gln	His	Gln	Arg	Val	His	Thr	Gly	Glu	Lys
				470					475					480
Pro	Tyr	Lys	Cys	Asn	Glu	Cys	Gly	Lys	Val	Phe	Asn	Gln	Lys	Ala
				485					490					495
Ser	Leu	Ala	Lys	His	Gln	Arg	Val	His	Thr	Ala	Glu	Lys	Pro	Tyr
				500					505					510
Lys	Cys	Asn	Glu	Cys	Gly	Lys	Ala	Phe	Thr	Gly	Gln	Ser	Thr	Leu
				515					520					525
Ile	His	His	Gln	Ala	Ile	His	Gly	Cys	Arg	Glu	Thr	Leu	Gln	Met
				530					535					540

&lt;210&gt; 22

&lt;211&gt; 549

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 619699CD1

&lt;400&gt; 22

Met	Leu	Glu	Asn	Tyr	Lys	Asn	Leu	Ala	Thr	Val	Gly	Tyr	Gln	Leu
1				5					10					15
Phe	Lys	Pro	Ser	Leu	Ile	Ser	Trp	Leu	Glu	Gln	Glu	Glu	Ser	Arg
				20					25					30
Thr	Val	Gln	Arg	Gly	Asp	Phe	Gln	Ala	Ser	Glu	Trp	Lys	Val	Gln
				35					40					45
Leu	Lys	Thr	Lys	Glu	Leu	Ala	Leu	Gln	Gln	Asp	Val	Leu	Gly	Glu
				50					55					60
Pro	Thr	Ser	Ser	Gly	Ile	Gln	Met	Ile	Gly	Ser	His	Asn	Gly	Gly
				65					70					75
Glu	Val	Ser	Asp	Val	Lys	Gln	Cys	Gly	Asp	Val	Ser	Ser	Glu	His
				80					85					90



Ser	Cys	Leu	Lys	Thr	His	Val	Arg	Thr	Gln	Asn	Ser	Glu	Asn	Thr	
				95					100						105
Phe	Glu	Cys	Tyr	Leu	Tyr	Gly	Val	Asp	Phe	Leu	Thr	Leu	His	Lys	
				110					115						120
Lys	Thr	Ser	Thr	Gly	Glu	Gln	Arg	Ser	Val	Phe	Ser	Gln	Cys	Gly	
				125					130						135
Lys	Ala	Phe	Ser	Leu	Asn	Pro	Asp	Val	Val	Cys	Gln	Arg	Thr	Cys	
				140					145						150
Thr	Gly	Glu	Lys	Ala	Phe	Asp	Cys	Ser	Asp	Ser	Gly	Lys	Ser	Phe	
				155					160						165
Ile	Asn	His	Ser	His	Leu	Gln	Gly	His	Leu	Arg	Thr	His	Asn	Gly	
				170					175						180
Glu	Ser	Leu	His	Glu	Trp	Lys	Glu	Cys	Gly	Arg	Gly	Phe	Ile	His	
				185					190						195
Ser	Thr	Asp	Leu	Ala	Val	Arg	Ile	Gln	Thr	His	Arg	Ser	Glu	Lys	
				200					205						210
Pro	Tyr	Lys	Cys	Lys	Glu	Cys	Gly	Lys	Gly	Phe	Arg	Tyr	Ser	Ala	
				215					220						225
Tyr	Leu	Asn	Ile	His	Met	Gly	Thr	His	Thr	Gly	Asp	Asn	Pro	Tyr	
				230					235						240
Glu	Cys	Lys	Glu	Cys	Gly	Lys	Ala	Phe	Thr	Arg	Ser	Cys	Gln	Leu	
				245					250						255
Thr	Gln	His	Arg	Lys	Thr	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	
				260					265						270
Lys	Asp	Cys	Gly	Arg	Ala	Phe	Thr	Val	Ser	Ser	Cys	Leu	Ser	Gln	
				275					280						285
His	Met	Lys	Ile	His	Val	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	Lys	Glu	
				290					295						300
Cys	Gly	Ile	Ala	Phe	Thr	Arg	Ser	Ser	Gln	Leu	Thr	Glu	His	Leu	
				305					310						315
Lys	Thr	His	Thr	Ala	Lys	Asp	Pro	Phe	Glu	Cys	Lys	Val	Cys	Gly	
				320					325						330
Lys	Ser	Phe	Arg	Asn	Ser	Ser	Cys	Leu	Ser	Asp	His	Phe	Arg	Ile	
				335					340						345
His	Thr	Gly	Ile	Lys	Pro	Tyr	Lys	Cys	Lys	Asp	Cys	Gly	Lys	Ala	
				350					355						360
Phe	Thr	Gln	Asn	Ser	Asp	Leu	Thr	Lys	His	Ala	Arg	Thr	His	Ser	
				365					370						375
Gly	Glu	Arg	Pro	Tyr	Glu	Cys	Lys	Glu	Cys	Gly	Lys	Ala	Phe	Ala	
				380					385						390
Arg	Ser	Ser	Arg	Leu	Ser	Glu	His	Thr	Arg	Thr	His	Thr	Gly	Glu	
				395					400						405
Lys	Pro	Phe	Glu	Cys	Val	Lys	Cys	Gly	Lys	Ala	Phe	Ala	Ile	Ser	
				410					415						420
Ser	Asn	Leu	Ser	Gly	His	Leu	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	
				425					430						435
Phe	Glu	Cys	Leu	Glu	Cys	Gly	Lys	Ala	Phe	Thr	His	Ser	Ser	Ser	
				440					445						450
Leu	Asn	Asn	His	Met	Arg	Thr	His	Ser	Ala	Lys	Lys	Pro	Phe	Thr	
				455					460						465
Cys	Met	Glu	Cys	Gly	Lys	Ala	Phe	Lys	Phe	Pro	Thr	Cys	Val	Asn	
				470					475						480
Leu	His	Met	Arg	Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Lys	Cys	Lys	
				485					490						495
Gln	Cys	Gly	Lys	Ser	Phe	Ser	Tyr	Ser	Asn	Ser	Phe	Gln	Leu	His	
				500					505						510
Glu	Arg	Thr	His	Thr	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	Lys	Glu	Cys	
				515					520						525
Gly	Lys	Ala	Phe	Ser	Ser	Ser	Ser	Ser	Phe	Arg	Asn	His	Glu	Arg	
				530					535						540
Arg	His	Ala	Asp	Glu	Arg	Leu	Ser	Ala							
				545											

<210> 23  
 <211> 361  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 693452CD1

<400> 23

Met	Ala	Asp	Phe	Lys	Val	Leu	Ser	Ser	Gln	Asp	Ile	Lys	Trp	Ala	
1				5					10					15	
Leu	His	Glu	Leu	Lys	Gly	His	Tyr	Ala	Ile	Thr	Arg	Lys	Ala	Leu	
				20					25					30	
Ser	Asp	Ala	Ile	Lys	Lys	Trp	Gln	Glu	Leu	Ser	Pro	Glu	Thr	Ser	
				35					40					45	
Gly	Lys	Arg	Lys	Lys	Arg	Lys	Gln	Met	Asn	Gln	Tyr	Ser	Tyr	Ile	
				50					55					60	
Asp	Phe	Lys	Phe	Glu	Gln	Gly	Asp	Ile	Lys	Ile	Glu	Lys	Arg	Met	
				65					70					75	
Phe	Phe	Leu	Glu	Asn	Lys	Arg	Arg	His	Cys	Arg	Ser	Tyr	Asp	Arg	
				80					85					90	
Arg	Ala	Leu	Leu	Pro	Ala	Val	Gln	Gln	Glu	Gln	Glu	Phe	Tyr	Glu	
				95					100					105	
Gln	Lys	Ile	Lys	Glu	Met	Ala	Glu	His	Glu	Asp	Phe	Leu	Leu	Ala	
				110					115					120	
Leu	Gln	Met	Asn	Glu	Glu	Gln	Tyr	Gln	Lys	Asp	Gly	Gln	Leu	Ile	
				125					130					135	
Glu	Cys	Arg	Cys	Cys	Tyr	Gly	Glu	Phe	Pro	Phe	Glu	Glu	Leu	Thr	
				140					145					150	
Gln	Cys	Ala	Asp	Ala	His	Leu	Phe	Cys	Lys	Glu	Cys	Leu	Ile	Arg	
				155					160					165	
Tyr	Ala	Gln	Glu	Ala	Val	Phe	Gly	Ser	Gly	Lys	Leu	Glu	Leu	Ser	
				170					175					180	
Cys	Met	Glu	Gly	Ser	Cys	Thr	Cys	Ser	Phe	Pro	Thr	Ser	Glu	Leu	
				185					190					195	
Glu	Lys	Val	Leu	Pro	Gln	Thr	Ile	Leu	Tyr	Lys	Tyr	Tyr	Glu	Arg	
				200					205					210	
Lys	Ala	Glu	Glu	Glu	Val	Ala	Ala	Ala	Tyr	Ala	Asp	Glu	Leu	Val	
				215					220					225	
Arg	Cys	Pro	Ser	Cys	Ser	Phe	Pro	Ala	Leu	Leu	Asp	Ser	Asp	Val	
				230					235					240	
Lys	Arg	Phe	Ser	Cys	Pro	Asn	Pro	His	Cys	Arg	Lys	Glu	Thr	Cys	
				245					250					255	
Arg	Lys	Cys	Gln	Gly	Leu	Trp	Lys	Glu	His	Asn	Gly	Leu	Thr	Cys	
				260					265					270	
Glu	Glu	Leu	Ala	Glu	Lys	Asp	Asp	Ile	Lys	Tyr	Arg	Thr	Ser	Ile	
				275					280					285	
Glu	Glu	Lys	Met	Thr	Ala	Ala	Arg	Ile	Arg	Lys	Cys	His	Lys	Cys	
				290					295					300	
Gly	Thr	Gly	Leu	Ile	Lys	Ser	Glu	Gly	Cys	Asn	Arg	Met	Ser	Cys	
				305					310					315	
Arg	Cys	Gly	Ala	Gln	Met	Cys	Tyr	Leu	Cys	Arg	Val	Ser	Ile	Asn	
				320					325					330	
Gly	Tyr	Asp	His	Xaa	Cys	Gln	Gln	Ser	Arg	Leu	Thr	Gly	Ala	Pro	
				335					340					345	
Phe	Gln	Gly	Val	Phe	Lys	Met	Leu	Ser	Met	Asp	Arg	Leu	Gln	Cys	
				350					355					360	
Lys															

<210> 24  
 <211> 241  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 839651CD1

<400> 24  
 Met Trp Pro Ser Leu Glu Ala Leu Cys Ser Leu Phe Ala Ala Arg  
 1 5 10 15  
 Ser Thr Gly Ser Gln Ala Gln Ser Ala Pro Thr Pro Ala Trp Asp  
 20 25 30  
 Glu Asp Thr Ala Gln Ile Gly Pro Lys Arg Ile Arg Lys Ala Ala  
 35 40 45  
 Lys Arg Glu Leu Met Pro Cys Asp Phe Pro Gly Cys Gly Arg Ile  
 50 55 60  
 Phe Ser Asn Arg Gln Tyr Leu Asn His His Lys Lys Tyr Gln His  
 65 70 75  
 Ile His Gln Lys Ser Phe Ser Cys Pro Glu Pro Ala Cys Gly Lys  
 80 85 90  
 Ser Phe Asn Phe Lys Lys His Leu Lys Glu His Met Lys Leu His  
 95 100 105  
 Ser Asp Thr Arg Asp Tyr Ile Cys Glu Phe Cys Ala Arg Ser Phe  
 110 115 120  
 Arg Thr Ser Ser Asn Leu Val Ile His Arg Arg Ile His Thr Gly  
 125 130 135  
 Glu Lys Pro Leu Gln Cys Glu Ile Cys Gly Phe Thr Cys Arg Gln  
 140 145 150  
 Lys Ala Ser Leu Asn Trp His Gln Arg Lys His Ala Glu Thr Val  
 155 160 165  
 Ala Ala Leu Arg Phe Pro Cys Glu Phe Cys Gly Lys Arg Phe Glu  
 170 175 180  
 Lys Pro Asp Ser Val Ala Ala His Arg Ser Lys Ser His Pro Ala  
 185 190 195  
 Leu Leu Leu Ala Pro Gln Glu Ser Pro Ser Gly Pro Leu Glu Pro  
 200 205 210  
 Cys Pro Ser Ile Ser Ala Pro Gly Pro Leu Gly Ser Ser Glu Gly  
 215 220 225  
 Ser Arg Pro Ser Ala Ser Pro Gln Ala Pro Thr Leu Leu Pro Gln  
 230 235 240  
 Gln

<210> 25  
 <211> 576  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1253545CD1

<400> 25  
 Met Ala Lys Ala Gln Glu Thr Gly His Leu Val Met Asp Val Arg  
 1 5 10 15  
 Arg Tyr Gly Lys Ala Gly Ser Pro Glu Thr Lys Trp Ile Asp Ala  
 20 25 30  
 Thr Ser Gly Ile Tyr Asn Ser Glu Lys Ser Ser Asn Leu Ser Val  
 35 40 45  
 Thr Thr Asp Phe Ser Glu Ser Leu Gln Ser Ser Asn Ile Glu Ser

	50		55		60
Lys Glu Ile Asn Gly	Ile His Asp Glu	Ser Asn Ala Phe Glu	Ser		
	65		70		75
Lys Ala Ser Glu Ser	Ile Ser Leu Lys	Asn Leu Lys Arg Arg	Ser		
	80		85		90
Gln Phe Phe Glu Gln	Gly Ser Ser Asp	Ser Val Val Pro Asp	Leu		
	95		100		105
Pro Val Pro Thr Ile	Ser Ala Pro Ser	Arg Trp Val Trp Asp	Gln		
	110		115		120
Glu Glu Glu Arg Lys	Arg Gln Glu Arg	Trp Gln Lys Glu Gln	Asp		
	125		130		135
Arg Leu Leu Gln Glu	Lys Tyr Gln Arg	Glu Gln Glu Lys Leu	Arg		
	140		145		150
Glu Glu Trp Gln Arg	Ala Lys Gln Glu	Ala Glu Arg Glu Asn	Ser		
	155		160		165
Lys Tyr Leu Asp Glu	Glu Leu Met Val	Leu Ser Ser Asn Ser	Met		
	170		175		180
Ser Leu Thr Thr Arg	Glu Pro Ser Leu	Ala Thr Trp Glu Ala	Thr		
	185		190		195
Trp Ser Glu Gly Ser	Lys Ser Ser Asp	Arg Glu Gly Thr Arg	Ala		
	200		205		210
Gly Glu Glu Glu Arg	Arg Gln Pro Gln	Glu Glu Val Val His	Glu		
	215		220		225
Asp Gln Gly Lys Lys	Pro Gln Asp Gln	Leu Val Ile Glu Arg	Glu		
	230		235		240
Arg Lys Trp Glu Gln	Gln Leu Gln Glu	Gln Gln Gln Lys	Arg		
	245		250		255
Leu Gln Ala Glu Ala	Glu Glu Gln Lys	Arg Pro Ala Glu Glu	Gln		
	260		265		270
Lys Arg Gln Ala Glu	Ile Glu Arg Glu	Thr Ser Val Arg Ile	Tyr		
	275		280		285
Gln Tyr Arg Arg Pro	Val Asp Ser Tyr	Asp Ile Pro Lys Thr	Glu		
	290		295		300
Glu Ala Ser Ser Gly	Phe Leu Pro Gly	Asp Arg Asn Lys Ser	Arg		
	305		310		315
Ser Thr Thr Glu Leu	Asp Asp Tyr Ser	Thr Asn Lys Asn Gly	Asn		
	320		325		330
Asn Lys Tyr Leu Asp	Gln Ile Gly Asn	Thr Thr Ser Ser Gln	Arg		
	335		340		345
Arg Ser Lys Lys Glu	Gln Val Pro Ser	Gly Ala Glu Leu Glu	Arg		
	350		355		360
Gln Gln Ile Leu Gln	Glu Met Arg Lys	Arg Thr Pro Leu His	Asn		
	365		370		375
Asp Asn Ser Trp Ile	Arg Gln Arg Ser	Ala Ser Val Asn Lys	Glu		
	380		385		390
Pro Val Ser Leu Pro	Gly Ile Met Arg	Arg Gly Glu Ser Leu	Asp		
	395		400		405
Asn Leu Asp Ser Pro	Arg Ser Asn Ser	Trp Arg Gln Pro Pro	Trp		
	410		415		420
Leu Asn Gln Pro Thr	Gly Phe Tyr Ala	Ser Ser Ser Val Gln	Asp		
	425		430		435
Phe Ser Arg Pro Gln	Pro Gln Leu Val	Ser Thr Ser Asn Arg	Ala		
	440		445		450
Tyr Met Arg Asn Pro	Ser Ser Ser Val	Pro Pro Pro Ser Ala	Gly		
	455		460		465
Ser Val Lys Thr Ser	Thr Thr Gly Val	Ala Thr Thr Gln Ser	Pro		
	470		475		480
Thr Pro Arg Ser His	Ser Pro Ser Ala	Ser Gln Ser Gly Ser	Gln		
	485		490		495
Leu Arg Asn Arg Ser	Val Ser Gly Lys	Arg Ile Cys Ser Tyr	Cys		
	500		505		510
Asn Asn Ile Leu Gly	Lys Gly Ala Ala	Met Ile Ile Glu Ser	Leu		
	515		520		525
Gly Leu Cys Tyr His	Leu His Cys Phe	Lys Cys Val Ala Cys	Glu		

	530		535		540
Cys Asp Leu Gly	Gly Ser Ser Ser Gly	Ala Glu Val Arg Ile Arg			
	545		550		555
Asn His Gln Leu	Tyr Cys Asn Asp Cys	Tyr Leu Arg Phe Lys Ser			
	560		565		570
Gly Arg Pro Thr	Ala Met				
	575				

<210> 26  
 <211> 408  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1425691CD1

<400> 26  
 Met Pro Gly His Leu Gln Glu Gly Phe Gly Cys Val Val Thr Asn  
 1 5 10 15  
 Arg Phe Asp Gln Leu Phe Asp Asp Glu Ser Asp Pro Phe Glu Val  
 20 25 30  
 Leu Lys Ala Ala Glu Asn Lys Lys Lys Glu Ala Gly Gly Gly Gly  
 35 40 45  
 Val Gly Gly Pro Gly Ala Lys Ser Ala Ala Gln Ala Ala Ala Gln  
 50 55 60  
 Thr Asn Ser Asn Ala Ala Gly Lys Gln Leu Arg Lys Glu Ser Gln  
 65 70 75  
 Lys Asp Arg Lys Asn Pro Leu Pro Pro Ser Val Gly Val Val Asp  
 80 85 90  
 Lys Lys Glu Glu Thr Gln Pro Pro Val Ala Leu Lys Lys Glu Gly  
 95 100 105  
 Ile Arg Arg Val Gly Arg Arg Pro Asp Gln Gln Leu Gln Gly Glu  
 110 115 120  
 Gly Lys Ile Ile Asp Arg Arg Pro Glu Arg Arg Pro Pro Arg Glu  
 125 130 135  
 Arg Arg Phe Glu Lys Pro Leu Glu Glu Lys Gly Glu Gly Gly Glu  
 140 145 150  
 Phe Ser Val Asp Arg Pro Ile Ile Asp Arg Pro Ile Arg Gly Arg  
 155 160 165  
 Gly Gly Leu Gly Arg Gly Arg Gly Gly Arg Gly Arg Gly Met Gly  
 170 175 180  
 Arg Gly Asp Gly Phe Asp Ser Arg Gly Lys Arg Glu Phe Asp Arg  
 185 190 195  
 His Ser Gly Ser Asp Arg Ser Ser Phe Ser His Tyr Ser Gly Leu  
 200 205 210  
 Lys His Glu Asp Lys Arg Gly Gly Ser Gly Ser His Asn Trp Gly  
 215 220 225  
 Thr Val Lys Asp Glu Leu Thr Glu Ser Pro Lys Tyr Ile Gln Lys  
 230 235 240  
 Gln Ile Ser Tyr Asn Tyr Ser Asp Leu Asp Gln Ser Asn Val Thr  
 245 250 255  
 Glu Glu Thr Pro Glu Gly Glu Glu His His Pro Val Ala Asp Thr  
 260 265 270  
 Glu Asn Lys Glu Asn Glu Val Glu Glu Val Lys Glu Glu Gly Pro  
 275 280 285  
 Lys Glu Met Thr Leu Asp Glu Trp Lys Ala Ile Gln Asn Lys Asp  
 290 295 300  
 Arg Ala Lys Val Glu Phe Asn Ile Arg Lys Pro Asn Glu Gly Ala  
 305 310 315  
 Asp Gly Gln Trp Lys Lys Gly Phe Val Leu His Lys Ser Lys Ser  
 320 325 330  
 Glu Glu Ala His Ala Glu Asp Ser Val Met Asp His His Phe Arg

	335		340		345
Lys Pro Ala Asn	Asp Ile Thr Ser Gln	Leu Glu Ile Asn Phe	Gly		
	350		355		360
Asp Leu Gly Arg	Pro Gly Arg Gly Gly	Arg Gly Gly Arg Gly	Gly		
	365		370		375
Arg Gly Arg Gly	Gly Arg Pro Asn Arg	Gly Ser Arg Thr Asp	Lys		
	380		385		390
Ser Ser Ala Ser	Ala Pro Asp Val Asp	Asp Pro Glu Ala Phe	Pro		
	395		400		405
Ala Leu Ala					

&lt;210&gt; 27

&lt;211&gt; 810

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1484257CD1

&lt;400&gt; 27

Met Asp Phe Pro Gln His Ser Gln His Val Leu Glu Gln Leu Asn		
1	5	10
Gln Gln Arg Gln Leu Gly Leu Leu Cys Asp Cys Thr Phe Val Val		15
	20	25
Asp Gly Val His Phe Lys Ala His Lys Ala Val Leu Ala Ala Cys		30
	35	40
Ser Glu Tyr Phe Lys Met Leu Phe Val Asp Gln Lys Asp Val Val		45
	50	55
His Leu Asp Ile Ser Asn Ala Ala Gly Leu Gly Gln Val Leu Glu		60
	65	70
Phe Met Tyr Thr Ala Lys Leu Ser Leu Ser Pro Glu Asn Val Asp		75
	80	85
Asp Val Leu Ala Val Ala Thr Phe Leu Gln Met Gln Asp Ile Ile		90
	95	100
Thr Ala Cys His Ala Leu Lys Ser Leu Ala Glu Pro Ala Thr Ser		105
	110	115
Pro Gly Gly Asn Ala Glu Ala Leu Ala Gln Lys Val Cys Pro Val		120
	125	130
Pro Ser Pro Gly Gly Asp Lys Arg Ala Lys Glu Glu Lys Val Ala		135
	140	145
Thr Ser Thr Leu Ser Arg Leu Glu Gln Ala Gly Arg Ser Thr Pro		150
	155	160
Ile Gly Pro Ser Arg Asp Leu Lys Glu Glu Arg Gly Gly Gln Ala		165
	170	175
Gln Ser Ala Ala Ser Gly Ala Glu Gln Thr Glu Lys Ala Asp Ala		180
	185	190
Pro Arg Glu Pro Pro Pro Val Glu Leu Lys Pro Asp Pro Thr Ser		195
	200	205
Gly Met Ala Ala Ala Glu Ala Glu Ala Ala Leu Ser Glu Ser Ser		210
	215	220
Glu Gln Glu Met Glu Val Glu Pro Ala Arg Lys Gly Glu Glu Glu		225
	230	235
Gln Lys Glu Gln Glu Glu Gln Glu Glu Glu Gly Ala Gly Pro Ala		240
	245	250
Glu Val Lys Glu Glu Gly Ser Gln Leu Glu Asn Gly Glu Ala Pro		255
	260	265
Glu Glu Asn Glu Asn Glu Glu Ser Ala Gly Thr Asp Ser Gly Gln		270
	275	280
Glu Leu Gly Ser Glu Ala Arg Gly Leu Arg Ser Gly Thr Tyr Gly		285
	290	295
Asp Arg Thr Glu Ser Lys Ala Tyr Gly Ser Val Ile His Lys Cys		300
	305	310
		315

Glu Asp Cys Gly	Lys Glu Phe Thr His	Thr Gly Asn Phe Lys Arg	320	325	330
His Ile Arg Ile	His Thr Gly Glu Lys	Pro Phe Ser Cys Arg Glu	335	340	345
Cys Ser Lys Ala	Phe Ser Asp Pro Ala	Ala Cys Glu Ala His Glu	350	355	360
Lys Thr His Ser	Pro Leu Lys Pro Tyr	Gly Cys Glu Glu Cys Gly	365	370	375
Lys Ser Tyr Arg	Leu Ile Ser Leu Leu	Asn Leu His Lys Lys Arg	380	385	390
His Ser Gly Glu	Ala Arg Tyr Arg Cys	Glu Asp Cys Gly Lys Leu	395	400	405
Phe Thr Thr Ser	Gly Asn Leu Lys Arg	His Gln Leu Val His Ser	410	415	420
Gly Glu Lys Pro	Tyr Gln Cys Asp Tyr	Cys Gly Arg Ser Phe Ser	425	430	435
Asp Pro Thr Ser	Lys Met Arg His Leu	Glu Thr His Asp Thr Asp	440	445	450
Lys Glu His Lys	Cys Pro His Cys Asp	Lys Lys Phe Asn Gln Val	455	460	465
Gly Asn Leu Lys	Ala His Leu Lys Ile	His Ile Ala Asp Gly Pro	470	475	480
Leu Lys Cys Arg	Glu Cys Gly Lys Gln	Phe Thr Thr Ser Gly Asn	485	490	495
Leu Lys Arg His	Leu Arg Ile His Ser	Gly Glu Lys Pro Tyr Val	500	505	510
Cys Ile His Cys	Gln Arg Gln Phe Ala	Asp Pro Gly Ala Leu Gln	515	520	525
Arg His Val Arg	Ile His Thr Gly Glu	Lys Pro Cys Gln Cys Val	530	535	540
Met Cys Gly Lys	Ala Phe Thr Gln Ala	Ser Ser Leu Ile Ala His	545	550	555
Val Arg Gln His	Thr Gly Glu Lys Pro	Tyr Val Cys Glu Arg Cys	560	565	570
Gly Lys Arg Phe	Val Gln Ser Ser Gln	Leu Ala Asn His Ile Arg	575	580	585
His His Asp Asn	Ile Arg Pro His Lys	Cys Ser Val Cys Ser Lys	590	595	600
Ala Phe Val Asn	Val Gly Asp Leu Ser	Lys His Ile Ile Ile His	605	610	615
Thr Gly Glu Lys	Pro Tyr Leu Cys Asp	Lys Cys Gly Arg Gly Phe	620	625	630
Asn Arg Val Asp	Asn Leu Arg Ser His	Val Lys Thr Val His Gln	635	640	645
Gly Lys Ala Gly	Ile Lys Ile Leu Glu	Pro Glu Glu Gly Ser Glu	650	655	660
Val Ser Val Val	Thr Val Asp Asp Met	Val Thr Leu Ala Thr Glu	665	670	675
Ala Leu Ala Ala	Thr Ala Val Thr Gln	Leu Thr Val Val Pro Val	680	685	690
Gly Ala Ala Val	Thr Ala Asp Glu Thr	Glu Val Leu Lys Ala Glu	695	700	705
Ile Ser Lys Ala	Val Lys Gln Val Gln	Glu Glu Asp Pro Asn Thr	710	715	720
His Ile Leu Tyr	Ala Cys Asp Ser Cys	Gly Asp Lys Phe Leu Asp	725	730	735
Ala Asn Ser Leu	Ala Gln His Val Arg	Ile His Thr Ala Gln Ala	740	745	750
Leu Val Met Phe	Gln Thr Asp Ala Asp	Phe Tyr Gln Gln Tyr Gly	755	760	765
Pro Gly Gly Thr	Trp Pro Ala Gly Gln	Val Leu Gln Ala Gly Glu	770	775	780
Leu Val Phe Arg	Pro Arg Asp Gly Ala	Glu Gly Gln Pro Ala Leu	785	790	795

Ala Glu Thr Ser Pro Thr Ala Pro Glu Cys Pro Pro Pro Ala Glu  
 800 805 810

<210> 28

<211> 324

<212> PRT

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte clone 1732368CD1

<400> 28

Met	Asp	Trp	Ser	Glu	Val	Lys	Glu	Glu	Lys	Asp	Asn	Leu	Glu	Ile	1	5	10	15
Lys	Gln	Glu	Glu	Lys	Phe	Val	Gly	Gln	Cys	Ile	Lys	Glu	Glu	Leu	20	25	30	35
Met	His	Gly	Glu	Cys	Val	Lys	Glu	Glu	Lys	Asp	Phe	Leu	Lys	Lys	40	45	50	55
Glu	Ile	Val	Asp	Asp	Thr	Lys	Val	Lys	Glu	Glu	Pro	Pro	Ile	Asn	60	65	70	75
His	Pro	Val	Gly	Cys	Lys	Arg	Lys	Leu	Ala	Met	Ser	Arg	Cys	Glu	80	85	90	95
Thr	Cys	Gly	Thr	Glu	Glu	Ala	Lys	Tyr	Arg	Cys	Pro	Arg	Cys	Met	100	105	110	115
Arg	Tyr	Ser	Cys	Ser	Leu	Pro	Cys	Val	Lys	Lys	His	Lys	Ala	Glu	120	125	130	135
Leu	Thr	Cys	Asn	Gly	Val	Arg	Asp	Lys	Thr	Ala	Tyr	Ile	Ser	Ile	140	145	150	155
Gln	Gln	Phe	Thr	Glu	Met	Asn	Leu	Leu	Ser	Asp	Tyr	Arg	Phe	Leu	160	165	170	175
Glu	Asp	Val	Ala	Arg	Thr	Ala	Asp	His	Ile	Ser	Arg	Asp	Ala	Phe	180	185	190	195
Leu	Lys	Arg	Pro	Ile	Ser	Asn	Lys	Tyr	Met	Tyr	Phe	Met	Lys	Asn	200	205	210	215
Arg	Ala	Arg	Arg	Gln	Gly	Ile	Asn	Leu	Lys	Leu	Leu	Pro	Asn	Gly	220	225	230	235
Phe	Thr	Lys	Arg	Lys	Glu	Asn	Ser	Thr	Phe	Phe	Asp	Lys	Lys	Lys	240	245	250	255
Gln	Gln	Phe	Cys	Trp	His	Val	Lys	Leu	Gln	Phe	Pro	Gln	Ser	Gln	260	265	270	275
Ala	Glu	Tyr	Ile	Glu	Lys	Arg	Val	Pro	Asp	Asp	Lys	Thr	Ile	Asn	280	285	290	295
Glu	Ile	Leu	Lys	Pro	Tyr	Ile	Asp	Pro	Glu	Lys	Ser	Asp	Pro	Val	300	305	310	315
Ile	Arg	Gln	Arg	Leu	Lys	Ala	Tyr	Ile	Arg	Ser	Gln	Thr	Gly	Val	320			
Gln	Ile	Leu	Met	Lys	Ile	Glu	Tyr	Met	Gln	Gln	Asn	Leu	Val	Arg				
Tyr	Tyr	Glu	Leu	Asp	Pro	Tyr	Lys	Ser	Leu	Leu	Asp	Asn	Leu	Arg				
Asn	Lys	Val	Ile	Ile	Glu	Tyr	Pro	Thr	Leu	His	Val	Val	Leu	Lys				
Gly	Ser	Asn	Asn	Asp	Met	Lys	Val	Leu	His	Gln	Val	Lys	Ser	Glu				
Ser	Thr	Lys	Asn	Val	Gly	Asn	Glu	Asn										

<210> 29

<211> 292



&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1870914CD1

&lt;400&gt; 29

```

Met Glu Glu Val Pro His Asp Cys Pro Gly Ala Asp Ser Ala Gln
 1          5          10          15
Ala Gly Arg Gly Ala Ser Cys Gln Gly Cys Pro Asn Gln Arg Leu
          20          25          30
Cys Ala Ser Gly Ala Gly Ala Thr Pro Asp Thr Ala Ile Glu Glu
          35          40          45
Ile Lys Glu Lys Met Lys Thr Val Lys His Lys Ile Leu Val Leu
          50          55          60
Ser Gly Lys Gly Gly Val Gly Lys Ser Thr Phe Ser Ala His Leu
          65          70          75
Ala His Gly Leu Ala Glu Asp Glu Asn Thr Gln Ile Ala Leu Leu
          80          85          90
Asp Ile Asp Ile Cys Gly Pro Ser Ile Pro Lys Ile Met Gly Leu
          95          100          105
Glu Gly Glu Gln Val His Gln Ser Gly Ser Gly Trp Ser Pro Val
          110          115          120
Tyr Val Glu Asp Asn Leu Gly Val Met Ser Val Gly Phe Leu Leu
          125          130          135
Ser Ser Pro Asp Asp Ala Val Ile Trp Arg Gly Pro Lys Lys Asn
          140          145          150
Gly Met Ile Lys Gln Phe Leu Arg Asp Val Asp Trp Gly Glu Val
          155          160          165
Asp Tyr Leu Ile Val Asp Thr Pro Pro Gly Thr Ser Asp Glu His
          170          175          180
Leu Ser Val Val Arg His Leu Ala Thr Ala His Ile Asp Gly Ala
          185          190          195
Val Ile Ile Thr Thr Pro Gln Glu Val Ser Leu Gln Asp Val Arg
          200          205          210
Lys Glu Ile Asn Phe Cys Arg Lys Val Lys Leu Pro Ile Ile Gly
          215          220          225
Val Val Glu Asn Met Ser Gly Phe Ile Cys Pro Lys Cys Lys Lys
          230          235          240
Glu Ser Gln Ile Phe Pro Pro Thr Thr Gly Gly Ala Glu Leu Met
          245          250          255
Cys Gln Asp Leu Glu Val Pro Leu Leu Gly Arg Val Pro Leu Asp
          260          265          270
Pro Leu Ile Gly Ile Gln Glu Phe Cys Asn Leu His Gln Ser Lys
          275          280          285
Glu Glu Asn Leu Ile Ser Ser
          290

```

&lt;210&gt; 30

&lt;211&gt; 259

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1910984CD1

&lt;400&gt; 30

```

Met Glu Cys His Leu Lys Thr His Tyr Lys Met Glu Tyr Lys Cys
 1          5          10          15
Arg Ile Cys Gln Thr Val Lys Ala Asn Gln Leu Glu Leu Glu Thr
          20          25          30

```

```

His Thr Arg Glu His Arg Leu Gly Asn His Tyr Lys Cys Asp Gln
  35                      40                      45
Cys Gly Tyr Leu Ser Lys Thr Ala Asn Lys Leu Ile Glu His Val
  50                      55                      60
Arg Val His Thr Gly Glu Arg Pro Phe His Cys Asp Gln Cys Ser
  65                      70                      75
Tyr Ser Cys Thr Gly Lys Asp Asn Leu Asn Leu His Lys Lys Leu
  80                      85                      90
Lys His Ala Pro Arg Gln Thr Phe Ser Cys Glu Glu Cys Leu Phe
  95                      100                     105
Lys Thr Thr His Pro Phe Val Phe Ser Arg His Val Lys Lys His
  110                     115                     120
Gln Ser Gly Asp Cys Pro Glu Glu Asp Lys Lys Gly Leu Cys Pro
  125                     130                     135
Ala Pro Lys Glu Pro Ala Gly Pro Gly Ala Pro Leu Leu Val Val
  140                     145                     150
Gly Ser Ser Arg Asn Leu Leu Ser Pro Leu Ser Val Met Ser Ala
  155                     160                     165
Ser Gln Ala Leu Gln Thr Val Ala Leu Ser Ala Ala His Gly Ser
  170                     175                     180
Ser Ser Glu Pro Asn Leu Ala Leu Lys Ala Leu Ala Phe Asn Gly
  185                     190                     195
Ser Pro Leu Arg Phe Asp Lys Tyr Arg Asn Ser Asp Phe Ala His
  200                     205                     210
Leu Ile Pro Leu Thr Met Leu Tyr Pro Lys Asn His Leu Asp Leu
  215                     220                     225
Thr Phe His Pro Pro Arg Pro Gln Thr Ala Pro Pro Ser Ile Pro
  230                     235                     240
Ser Pro Lys His Ser Phe Leu Ala Tyr Leu Gly Leu Arg Glu Arg
  245                     250                     255
Ala Glu Thr Val

```

&lt;210&gt; 31

&lt;211&gt; 97

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1943040CD1

&lt;400&gt; 31

```

Met Glu His His Ser Ser His Gly Gly Arg Lys Arg Tyr Ala Cys
  1                      5                      10                      15
Gln Gly Cys Trp Lys Thr Phe His Phe Ser Leu Ala Leu Ala Glu
  20                      25                      30
His Gln Lys Thr His Glu Lys Glu Lys Ser Tyr Ala Leu Gly Gly
  35                      40                      45
Ala Arg Gly Pro Gln Pro Ser Thr Arg Glu Pro Arg Arg Gly Leu
  50                      55                      60
Gly Arg Ala Val Pro Gln Arg Ala Trp Arg Ala Arg Leu Pro Pro
  65                      70                      75
His Pro Gln Arg Arg Arg Gly Glu Pro Leu Cys Cys Pro Val Pro
  80                      85                      90
Glu Gly Pro Leu Cys Arg Pro
  95

```

&lt;210&gt; 32

&lt;211&gt; 812

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2076520CD1

&lt;400&gt; 32

```

Met Ile Glu Pro Asp Gln Cys Phe Cys Arg Phe Asp Leu Thr Gly
 1           5           10           15
Thr Cys Asn Asp Asp Asp Cys Gln Trp Gln His Ile Gln Asp Tyr
          20           25           30
Thr Leu Ser Arg Lys Gln Leu Phe Gln Asp Ile Leu Ser Tyr Asn
          35           40           45
Leu Ser Leu Ile Gly Cys Ala Glu Thr Ser Thr Asn Glu Glu Ile
          50           55           60
Thr Ala Ser Ala Glu Lys Tyr Val Glu Lys Leu Phe Gly Val Asn
          65           70           75
Lys Asp Arg Met Ser Met Asp Gln Met Ala Val Leu Leu Val Ser
          80           85           90
Asn Ile Asn Glu Ser Lys Gly His Thr Pro Pro Phe Thr Thr Tyr
          95          100          105
Lys Asp Lys Arg Lys Trp Lys Pro Lys Phe Trp Arg Lys Pro Ile
          110          115          120
Ser Asp Asn Ser Phe Ser Ser Asp Glu Glu Gln Ser Thr Gly Pro
          125          130          135
Ile Lys Tyr Ala Phe Gln Pro Glu Asn Gln Ile Asn Val Pro Ala
          140          145          150
Leu Asp Thr Val Val Thr Pro Asp Asp Val Arg Tyr Phe Thr Asn
          155          160          165
Glu Thr Asp Asp Ile Ala Asn Leu Glu Ala Ser Val Leu Glu Asn
          170          175          180
Pro Ser His Val Gln Leu Trp Leu Lys Leu Ala Tyr Lys Tyr Leu
          185          190          195
Asn Gln Asn Glu Gly Glu Cys Ser Glu Ser Leu Asp Ser Ala Leu
          200          205          210
Asn Val Leu Ala Arg Ala Leu Glu Asn Asn Lys Asp Asn Pro Glu
          215          220          225
Ile Trp Cys His Tyr Leu Arg Leu Phe Ser Lys Arg Gly Thr Lys
          230          235          240
Asp Glu Val Gln Glu Met Cys Glu Thr Ala Val Glu Tyr Ala Pro
          245          250          255
Asp Tyr Gln Ser Phe Trp Thr Phe Leu His Leu Glu Ser Thr Phe
          260          265          270
Glu Glu Lys Asp Tyr Val Cys Glu Arg Met Leu Glu Phe Leu Met
          275          280          285
Gly Ala Ala Lys Gln Glu Thr Ser Asn Ile Leu Ser Phe Gln Leu
          290          295          300
Leu Glu Ala Leu Leu Phe Arg Val Gln Leu His Ile Phe Thr Gly
          305          310          315
Arg Cys Gln Ser Ala Leu Ala Ile Leu Gln Asn Ala Leu Lys Ser
          320          325          330
Ala Asn Asp Gly Ile Val Ala Glu Tyr Leu Lys Thr Ser Asp Arg
          335          340          345
Cys Leu Ala Trp Leu Ala Tyr Ile His Leu Ile Glu Phe Asn Ile
          350          355          360
Leu Pro Ser Lys Phe Tyr Asp Pro Ser Asn Asp Asn Pro Ser Arg
          365          370          375
Ile Val Asn Thr Glu Ser Phe Val Met Pro Trp Gln Ala Val Gln
          380          385          390
Asp Val Lys Thr Asn Pro Asp Met Leu Leu Ala Val Phe Glu Asp
          395          400          405
Ala Val Lys Ala Cys Thr Asp Glu Ser Leu Ala Val Glu Glu Arg
          410          415          420
Ile Glu Ala Cys Leu Pro Leu Tyr Thr Asn Met Ile Ala Leu His
          425          430          435
Gln Leu Leu Glu Arg Tyr Glu Ala Ala Met Glu Leu Cys Lys Ser

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Leu Leu Glu Ser Cys Pro Ile Asn Cys Gln Leu Leu Glu Ala Leu	440	445	450
Val Ala Leu Tyr Leu Gln Thr Asn Gln His Asp Lys Ala Arg Ala	455	460	465
Val Trp Leu Thr Ala Phe Glu Lys Asn Pro Gln Asn Ala Glu Val	470	475	480
Phe Tyr His Met Cys Lys Phe Phe Ile Leu Gln Asn Arg Gly Asp	485	490	495
Asn Leu Leu Pro Phe Leu Arg Lys Phe Ile Ala Ser Phe Phe Lys	500	505	510
Pro Gly Phe Glu Lys Tyr Asn Asn Leu Asp Leu Phe Arg Tyr Leu	515	520	525
Leu Asn Ile Pro Gly Pro Ile Asp Ile Pro Ser Arg Leu Cys Lys	530	535	540
Gly Asn Phe Asp Asp Asp Met Phe Asn His Gln Val Pro Tyr Leu	545	550	555
Trp Leu Ile Tyr Cys Leu Cys His Pro Leu Gln Ser Ser Ile Lys	560	565	570
Glu Thr Val Glu Ala Tyr Glu Ala Ala Leu Gly Val Ala Met Arg	575	580	585
Cys Asp Ile Val Gln Lys Ile Trp Met Asp Tyr Leu Val Phe Ala	590	595	600
Asn Asn Arg Ala Ala Gly Ser Arg Asn Lys Val Gln Glu Phe Arg	605	610	615
Phe Phe Thr Asp Leu Val Asn Arg Cys Leu Val Thr Val Pro Ala	620	625	630
Arg Tyr Pro Ile Pro Phe Ser Ser Ala Asp Tyr Trp Ser Asn Tyr	635	640	645
Glu Phe His Asn Arg Val Ile Phe Phe Tyr Leu Ser Cys Val Pro	650	655	660
Lys Thr Gln His Ser Lys Thr Leu Glu Arg Phe Cys Ser Val Met	665	670	675
Pro Ala Asn Ser Gly Leu Ala Leu Arg Leu Leu Gln His Glu Trp	680	685	690
Glu Glu Ser Asn Val Gln Ile Leu Lys Leu Gln Ala Lys Met Phe	695	700	705
Thr Tyr Asn Ile Pro Thr Cys Leu Ala Thr Trp Lys Ile Ala Ile	710	715	720
Ala Ala Glu Ile Val Leu Lys Gly Gln Arg Glu Val His Arg Leu	725	730	735
Tyr Gln Arg Ala Leu Gln Lys Leu Pro Leu Cys Ala Ser Leu Trp	740	745	750
Lys Asp Gln Leu Leu Phe Glu Ala Ser Glu Gly Gly Lys Thr Asp	755	760	765
Asn Leu Arg Lys Leu Val Ser Lys Cys Gln Glu Ile Gly Val Ser	770	775	780
Leu Asn Glu Leu Leu Asn Leu Asn Ser Asn Lys Thr Glu Ser Lys	785	790	795
Asn His	800	805	810

&lt;210&gt; 33

&lt;211&gt; 392

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2291241CD1

&lt;400&gt; 33

Met Asp Ala Leu Val Glu Asp Asp Ile Cys Ile Leu Asn His Glu

1	5	10	15
Lys Ala His Lys Arg Asp Thr Val Thr Pro Val Ser Ile Tyr Ser			
	20	25	30
Gly Asp Glu Ser Val Ala Ser His Phe Ala Leu Val Thr Ala Tyr			
	35	40	45
Glu Asp Ile Lys Lys Arg Leu Lys Asp Ser Glu Lys Glu Asn Ser			
	50	55	60
Leu Leu Lys Lys Arg Ile Arg Phe Leu Glu Glu Lys Leu Ile Ala			
	65	70	75
Arg Phe Glu Glu Glu Thr Ser Ser Val Gly Arg Glu Gln Val Asn			
	80	85	90
Lys Ala Tyr His Ala Tyr Arg Glu Val Cys Ile Asp Arg Asp Asn			
	95	100	105
Leu Lys Ser Lys Leu Asp Lys Met Asn Lys Asp Asn Ser Glu Ser			
	110	115	120
Leu Lys Val Leu Asn Glu Gln Leu Gln Ser Lys Glu Val Glu Leu			
	125	130	135
Leu Gln Leu Arg Thr Glu Val Glu Thr Gln Gln Val Met Arg Asn			
	140	145	150
Leu Asn Pro Pro Ser Ser Asn Trp Glu Val Glu Lys Leu Ser Cys			
	155	160	165
Asp Leu Lys Ile His Gly Leu Glu Gln Glu Leu Glu Leu Met Arg			
	170	175	180
Lys Glu Cys Ser Asp Leu Lys Ile Glu Leu Gln Lys Ala Lys Gln			
	185	190	195
Thr Asp Pro Tyr Gln Glu Asp Asn Leu Lys Ser Arg Asp Leu Gln			
	200	205	210
Lys Leu Ser Ile Ser Ser Asp Asn Met Gln His Ala Tyr Trp Glu			
	215	220	225
Leu Lys Arg Glu Met Ser Asn Leu His Leu Val Thr Gln Val Gln			
	230	235	240
Ala Glu Leu Leu Arg Lys Leu Lys Thr Ser Thr Ala Ile Lys Lys			
	245	250	255
Ala Cys Ala Pro Val Gly Cys Ser Glu Asp Leu Gly Arg Asp Ser			
	260	265	270
Thr Lys Leu His Leu Met Asn Phe Thr Ala Thr Tyr Thr Arg His			
	275	280	285
Pro Pro Leu Leu Pro Asn Gly Lys Ala Leu Cys His Thr Thr Ser			
	290	295	300
Ser Pro Leu Pro Gly Asp Val Lys Val Leu Ser Glu Lys Ala Ile			
	305	310	315
Leu Gln Ser Trp Thr Asp Asn Glu Arg Ser Ile Pro Asn Asp Gly			
	320	325	330
Thr Cys Phe Gln Glu His Ser Ser Tyr Gly Arg Asn Ser Leu Glu			
	335	340	345
Asp Asn Ser Trp Val Phe Pro Ser Pro Pro Lys Ser Ser Glu Thr			
	350	355	360
Ala Phe Gly Glu Thr Lys Thr Lys Thr Leu Pro Leu Pro Asn Leu			
	365	370	375
Pro Pro Leu His Tyr Leu Asp Gln His Asn Gln Asn Cys Leu Tyr			
	380	385	390
Lys Asn			

&lt;210&gt; 34

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2329692CD1

&lt;400&gt; 34

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Met Ile Tyr Phe Phe Ile Ile Ile Val Glu Tyr Phe Tyr Gly Lys
 1           5           10           15
Ile Phe Val Val Leu Ile Ile Pro Ile Lys Ile Met Pro Asn Thr
           20           25           30
Lys Tyr Glu Phe Tyr Asp Val His Phe Val Leu Gly Ile Lys Arg
           35           40           45
Lys Lys His Thr Ser Trp Lys Ser Val Ser Cys Phe Leu Leu Leu
           50           55           60

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&lt;210&gt; 35

&lt;211&gt; 209

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2474110CD1

&lt;400&gt; 35

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Met Asp Pro Ser Asp Ile Tyr Ala Val Ile Gln Ile Pro Gly Ser
 1           5           10           15
Arg Glu Phe Asp Val Ser Phe Arg Ser Ala Glu Lys Leu Ala Leu
           20           25           30
Phe Leu Arg Val Tyr Glu Glu Lys Arg Glu Gln Glu Asp Cys Trp
           35           40           45
Glu Asn Phe Val Val Leu Gly Arg Ser Lys Ser Ser Leu Lys Thr
           50           55           60
Leu Phe Ile Leu Phe Arg Asn Glu Thr Val Asp Val Glu Asp Ile
           65           70           75
Val Thr Trp Leu Lys Arg His Cys Asp Val Leu Ala Val Pro Val
           80           85           90
Lys Val Thr Asp Arg Phe Gly Ile Trp Thr Gly Glu Tyr Lys Cys
           95          100          105
Glu Ile Glu Leu Arg Gln Gly Glu Gly Val Arg His Leu Pro
          110          115          120
Gly Ala Phe Phe Leu Gly Ala Glu Arg Gly Tyr Ser Trp Tyr Lys
          125          130          135
Gly Gln Pro Lys Thr Cys Phe Lys Cys Gly Ser Arg Thr His Met
          140          145          150
Ser Gly Ser Cys Thr Gln Asp Arg Cys Phe Arg Cys Arg Glu Glu
          155          160          165
Gly His Leu Ser Pro Tyr Cys Arg Lys Gly Ile Val Cys Asn Leu
          170          175          180
Cys Gly Lys Arg Gly His Ala Phe Ala Gln Cys Pro Lys Ala Val
          185          190          195
His Asn Ser Val Ala Ala Gln Leu Thr Gly Val Ala Gly His
          200          205

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&lt;210&gt; 36

&lt;211&gt; 257

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2495790CD1

&lt;400&gt; 36

```

Met Val Gly Ala Gly Ile Ser Thr Pro Ser Gly Ile Pro Asp Phe
 1           5           10           15

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Arg Ser Pro Gly Ser Gly Leu Tyr Ser Asn Leu Gln Gln Tyr Asp  
 20 25 30  
 Leu Pro Tyr Pro Glu Ala Ile Phe Glu Leu Pro Phe Phe Phe His  
 35 40 45  
 Asn Pro Lys Pro Phe Phe Thr Leu Ala Lys Glu Leu Tyr Pro Gly  
 50 55 60  
 Asn Tyr Lys Pro Asn Val Thr His Tyr Phe Leu Arg Leu Leu His  
 65 70 75  
 Asp Lys Gly Leu Leu Leu Arg Leu Tyr Thr Gln Asn Ile Asp Gly  
 80 85 90  
 Leu Glu Arg Val Ser Gly Ile Pro Ala Ser Lys Leu Val Glu Ala  
 95 100 105  
 His Gly Thr Phe Ala Ser Ala Thr Cys Thr Val Cys Gln Arg Pro  
 110 115 120  
 Phe Pro Gly Glu Asp Ile Arg Ala Asp Val Met Ala Asp Arg Val  
 125 130 135  
 Pro Arg Cys Pro Val Cys Thr Gly Val Val Lys Pro Asp Ile Val  
 140 145 150  
 Phe Phe Gly Glu Pro Leu Pro Gln Arg Phe Leu Leu His Val Val  
 155 160 165  
 Asp Phe Pro Met Ala Asp Leu Leu Leu Ile Leu Gly Thr Ser Leu  
 170 175 180  
 Glu Val Glu Pro Phe Ala Ser Leu Thr Glu Ala Val Arg Ser Ser  
 185 190 195  
 Val Pro Arg Leu Leu Ile Asn Arg Asp Leu Val Gly Pro Leu Ala  
 200 205 210  
 Trp His Pro Arg Ser Arg Asp Val Ala Gln Leu Gly Asp Val Val  
 215 220 225  
 His Gly Val Glu Ser Leu Val Glu Leu Leu Gly Trp Thr Glu Glu  
 230 235 240  
 Met Arg Asp Leu Val Gln Arg Glu Thr Gly Lys Leu Asp Gly Pro  
 245 250 255  
 Asp Lys

&lt;210&gt; 37

&lt;211&gt; 138

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2661254CD1

&lt;400&gt; 37

Met Ala Thr Lys Arg Leu Phe Gly Ala Thr Arg Thr Trp Ala Gly  
 1 5 10 15  
 Trp Gly Ala Trp Glu Leu Leu Asn Pro Ala Thr Ser Gly Arg Leu  
 20 25 30  
 Leu Ala Arg Asp Tyr Ala Lys Lys Pro Val Met Lys Gly Ala Lys  
 35 40 45  
 Ser Gly Lys Gly Ala Val Thr Ser Glu Ala Leu Lys Asp Pro Asp  
 50 55 60  
 Val Cys Thr Asp Pro Val Gln Leu Thr Thr Tyr Ala Met Gly Val  
 65 70 75  
 Asn Ile Tyr Lys Glu Gly Gln Asp Val Pro Leu Lys Pro Asp Ala  
 80 85 90  
 Glu Tyr Pro Glu Trp Leu Phe Glu Met Asn Leu Gly Pro Pro Lys  
 95 100 105  
 Thr Leu Glu Glu Leu Asp Pro Glu Ser Arg Glu Tyr Trp Arg Arg  
 110 115 120  
 Leu Arg Lys Gln Asn Ile Trp Arg His Asn Arg Leu Ser Lys Asn  
 125 130 135

Lys Arg Leu

&lt;210&gt; 38

&lt;211&gt; 999

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2674047CD1

&lt;400&gt; 38

Met	Gly	Pro	Ser	Arg	Leu	Arg	Leu	Gly	Phe	Phe	Xaa	Lys	Arg	Gly	1	5	10	15
Cys	Ser	Arg	Ala	Met	Val	Glu	Ile	Glu	Leu	Phe	Arg	Ala	Ser	Gly	20	25	30	
Asn	Leu	Val	Ile	Thr	Arg	Glu	Ile	Asp	Val	Ala	Lys	Asn	Gln	Ser	35	40	45	
Phe	Trp	Phe	Ile	Asn	Lys	Lys	Ser	Thr	Thr	Gln	Xaa	Ile	Val	Glu	50	55	60	
Glu	Lys	Val	Ala	Ala	Leu	Asn	Ile	Gln	Val	Gly	Asn	Leu	Cys	Gln	65	70	75	
Phe	Leu	Pro	Gln	Asp	Lys	Val	Gly	Glu	Phe	Ala	Lys	Leu	Ser	Lys	80	85	90	
Ile	Glu	Leu	Leu	Glu	Ala	Thr	Glu	Lys	Ser	Ile	Gly	Pro	Pro	Glu	95	100	105	
Met	His	Lys	Tyr	His	Cys	Glu	Leu	Lys	Asn	Leu	Arg	Glu	Lys	Glu	110	115	120	
Lys	Gln	Leu	Glu	Thr	Ser	Cys	Lys	Glu	Lys	Thr	Glu	Tyr	Leu	Gln	125	130	135	
Lys	Met	Val	Gln	Arg	Asn	Glu	Arg	Tyr	Lys	Gln	Asp	Val	Glu	Arg	140	145	150	
Phe	Tyr	Glu	Arg	Lys	Arg	His	Leu	Asp	Leu	Ile	Glu	Met	Leu	Glu	155	160	165	
Ala	Lys	Arg	Pro	Trp	Val	Glu	Tyr	Glu	Asn	Val	Arg	Gln	Glu	Tyr	170	175	180	
Glu	Glu	Val	Lys	Leu	Val	Arg	Asp	Arg	Val	Lys	Glu	Glu	Val	Arg	185	190	195	
Lys	Leu	Lys	Glu	Gly	Gln	Ile	Pro	Ile	Thr	Cys	Arg	Ile	Glu	Glu	200	205	210	
Met	Glu	Asn	Glu	Arg	His	Asn	Leu	Glu	Ala	Arg	Ile	Lys	Glu	Lys	215	220	225	
Ala	Thr	Asp	Ile	Lys	Glu	Ala	Ser	Gln	Lys	Cys	Lys	Gln	Lys	Gln	230	235	240	
Asp	Val	Ile	Glu	Arg	Lys	Asp	Lys	His	Ile	Glu	Glu	Leu	Gln	Gln	245	250	255	
Ala	Leu	Ile	Val	Lys	Gln	Asn	Glu	Glu	Leu	Asp	Arg	Gln	Arg	Arg	260	265	270	
Ile	Gly	Asn	Thr	Arg	Lys	Met	Ile	Glu	Asp	Leu	Gln	Asn	Glu	Leu	275	280	285	
Lys	Thr	Thr	Glu	Asn	Cys	Glu	Asn	Leu	Gln	Pro	Gln	Ile	Asp	Ala	290	295	300	
Ile	Thr	Asn	Asp	Leu	Arg	Arg	Ile	Gln	Asp	Glu	Lys	Ala	Leu	Cys	305	310	315	
Glu	Gly	Glu	Ile	Ile	Asp	Lys	Arg	Arg	Glu	Arg	Glu	Thr	Leu	Glu	320	325	330	
Lys	Glu	Lys	Lys	Ser	Val	Asp	Asp	His	Ile	Val	Arg	Phe	Asp	Asn	335	340	345	
Leu	Met	Asn	Gln	Lys	Glu	Asp	Lys	Leu	Arg	Gln	Arg	Phe	Arg	Asp	350	355	360	
Thr	Tyr	Asp	Ala	Val	Leu	Trp	Leu	Arg	Asn	Asn	Arg	Asp	Lys	Phe	365	370	375	



Lys	Gln	Arg	Val	Cys	Glu	Pro	Ile	Met	Leu	Thr	Ile	Asn	Met	Lys	
				380					385					390	
Asp	Asn	Lys	Asn	Ala	Lys	Tyr	Ile	Glu	Asn	His	Ile	Pro	Ser	Asn	
				395					400					405	
Asp	Leu	Arg	Ala	Phe	Val	Phe	Glu	Ser	Gln	Glu	Asp	Met	Glu	Val	
				410					415					420	
Phe	Leu	Lys	Glu	Val	Arg	Asp	Asn	Lys	Lys	Leu	Arg	Val	Asn	Ala	
				425					430					435	
Val	Ile	Ala	Pro	Lys	Ser	Ser	Tyr	Ala	Asp	Lys	Ala	Pro	Ser	Arg	
				440					445					450	
Ser	Leu	Asn	Glu	Leu	Lys	Gln	Tyr	Gly	Phe	Phe	Ser	Tyr	Leu	Arg	
				455					460					465	
Glu	Leu	Phe	Asp	Ala	Pro	Asp	Pro	Val	Met	Ser	Tyr	Leu	Cys	Cys	
				470					475					480	
Gln	Tyr	His	Ile	His	Glu	Val	Pro	Val	Gly	Thr	Glu	Lys	Thr	Arg	
				485					490					495	
Glu	Arg	Ile	Glu	Arg	Val	Ile	Gln	Glu	Thr	Arg	Leu	Lys	Gln	Ile	
				500					505					510	
Tyr	Thr	Ala	Glu	Glu	Lys	Tyr	Val	Val	Lys	Thr	Ser	Phe	Tyr	Ser	
				515					520					525	
Asn	Lys	Val	Ile	Ser	Ser	Asn	Thr	Ser	Leu	Lys	Val	Ala	Gln	Phe	
				530					535					540	
Leu	Thr	Val	Thr	Val	Asp	Leu	Glu	Gln	Arg	Arg	His	Leu	Glu	Glu	
				545					550					555	
Gln	Leu	Lys	Glu	Ile	His	Arg	Lys	Leu	Gln	Ala	Val	Asp	Ser	Gly	
				560					565					570	
Leu	Ile	Ala	Leu	Arg	Glu	Thr	Ser	Lys	His	Leu	Glu	His	Lys	Asp	
				575					580					585	
Asn	Glu	Leu	Arg	Gln	Lys	Lys	Lys	Glu	Leu	Leu	Glu	Arg	Lys	Thr	
				590					595					600	
Lys	Lys	Arg	Gln	Leu	Glu	Gln	Lys	Ile	Ser	Ser	Lys	Leu	Gly	Ser	
				605					610					615	
Leu	Lys	Leu	Met	Glu	Gln	Asp	Thr	Cys	Asn	Leu	Glu	Glu	Glu	Glu	
				620					625					630	
Arg	Lys	Ala	Ser	Thr	Lys	Ile	Lys	Glu	Ile	Asn	Val	Gln	Lys	Ala	
				635					640					645	
Lys	Leu	Val	Thr	Glu	Leu	Thr	Asn	Leu	Ile	Lys	Ile	Cys	Thr	Ser	
				650					655					660	
Leu	His	Ile	Gln	Lys	Val	Asp	Leu	Ile	Leu	Gln	Asn	Thr	Thr	Val	
				665					670					675	
Ile	Ser	Glu	Lys	Asn	Lys	Leu	Glu	Ser	Asp	Tyr	Met	Ala	Ala	Ser	
				680					685					690	
Ser	Gln	Leu	Arg	Leu	Thr	Glu	Gln	His	Phe	Ile	Glu	Leu	Asp	Glu	
				695					700					705	
Asn	Arg	Gln	Arg	Leu	Leu	Gln	Lys	Cys	Lys	Glu	Leu	Met	Lys	Arg	
				710					715					720	
Ala	Arg	Gln	Val	Cys	Asn	Leu	Gly	Ala	Glu	Gln	Thr	Leu	Pro	Gln	
				725					730					735	
Glu	Tyr	Gln	Thr	Gln	Val	Pro	Thr	Ile	Pro	Asn	Gly	His	Asn	Ser	
				740					745					750	
Ser	Leu	Pro	Met	Val	Phe	Gln	Asp	Leu	Pro	Asn	Thr	Leu	Asp	Glu	
				755					760					765	
Ile	Asp	Ala	Leu	Leu	Thr	Glu	Glu	Arg	Ser	Arg	Ala	Ser	Cys	Phe	
				770					775					780	
Thr	Gly	Leu	Asn	Pro	Thr	Ile	Val	Gln	Glu	Tyr	Thr	Lys	Arg	Glu	
				785					790					795	
Glu	Glu	Ile	Glu	Gln	Leu	Thr	Glu	Glu	Leu	Lys	Gly	Lys	Lys	Val	
				800					805					810	
Glu	Leu	Asp	Gln	Tyr	Arg	Glu	Asn	Ile	Ser	Gln	Val	Lys	Glu	Arg	
				815					820					825	
Trp	Leu	Asn	Pro	Leu	Lys	Glu	Leu	Val	Glu	Lys	Ile	Asn	Glu	Lys	
				830					835					840	
Phe	Ser	Asn	Phe	Phe	Ser	Ser	Met	Gln	Cys	Ala	Gly	Glu	Val	Asp	
				845					850					855	

Leu	His	Thr	Glu	Asn	Glu	Glu	Asp	Tyr	Asp	Lys	Tyr	Gly	Ile	Arg	
				860					865						870
Ile	Arg	Val	Lys	Phe	Arg	Ser	Ser	Thr	Gln	Leu	His	Glu	Leu	Thr	
				875					880						885
Pro	His	His	Gln	Ser	Gly	Gly	Glu	Arg	Ser	Val	Ser	Thr	Met	Leu	
				890					895						900
Tyr	Leu	Met	Ala	Leu	Gln	Glu	Leu	Asn	Arg	Cys	Pro	Phe	Arg	Val	
				905					910						915
Val	Asp	Glu	Ile	Asn	Gln	Gly	Met	Asp	Pro	Ile	Asn	Glu	Arg	Arg	
				920					925						930
Val	Phe	Glu	Met	Val	Val	Asn	Thr	Ala	Cys	Lys	Glu	Asn	Thr	Ser	
				935					940						945
Gln	Tyr	Phe	Phe	Ile	Thr	Pro	Lys	Leu	Leu	Gln	Asn	Leu	Pro	Tyr	
				950					955						960
Ser	Glu	Lys	Met	Thr	Val	Leu	Phe	Val	Tyr	Asn	Gly	Pro	His	Met	
				965					970						975
Leu	Glu	Pro	Asn	Thr	Trp	Asn	Leu	Lys	Ala	Phe	Gln	Arg	Arg	Arg	
				980					985						990
Arg	Arg	Ile	Thr	Phe	Thr	Gln	Pro	Ser							
				995											

&lt;210&gt; 39

&lt;211&gt; 377

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2762174CD1

&lt;400&gt; 39

Met	Ala	Glu	Leu	Glu	Ser	His	Pro	Cys	Asp	Ile	Cys	Gly	Pro	Ile	
1				5					10						15
Leu	Lys	Asp	Thr	Leu	His	Leu	Ala	Lys	Tyr	His	Gly	Gly	Lys	Ala	
				20					25						30
Arg	Gln	Lys	Pro	Tyr	Leu	Cys	Gly	Ala	Cys	Gly	Lys	Gln	Phe	Trp	
				35					40						45
Phe	Ser	Thr	Asp	Phe	Asp	Gln	His	Gln	Asn	Gln	Pro	Asn	Gly	Gly	
				50					55						60
Lys	Leu	Phe	Pro	Arg	Lys	Glu	Gly	Arg	Asp	Ser	Val	Lys	Ser	Cys	
				65					70						75
Arg	Val	His	Val	Pro	Glu	Lys	Thr	Leu	Thr	Cys	Gly	Lys	Gly	Arg	
				80					85						90
Arg	Asp	Phe	Ser	Ala	Thr	Ser	Gly	Leu	Leu	Gln	His	Gln	Ala	Ser	
				95					100						105
Leu	Ser	Ser	Met	Lys	Pro	His	Lys	Ser	Thr	Lys	Leu	Val	Ser	Gly	
				110					115						120
Phe	Leu	Met	Gly	Gln	Arg	Tyr	His	Arg	Cys	Gly	Glu	Cys	Gly	Lys	
				125					130						135
Ala	Phe	Thr	Arg	Lys	Asp	Thr	Leu	Ala	Arg	His	Gln	Arg	Ile	His	
				140					145						150
Thr	Gly	Glu	Arg	Pro	Tyr	Glu	Cys	Asn	Glu	Cys	Gly	Lys	Phe	Phe	
				155					160						165
Ser	Gln	Ser	Tyr	Asp	Leu	Phe	Lys	His	Gln	Thr	Val	His	Thr	Gly	
				170					175						180
Glu	Arg	Pro	Tyr	Glu	Cys	Ser	Glu	Cys	Gly	Lys	Phe	Phe	Arg	Gln	
				185					190						195
Ile	Ser	Gly	Leu	Ile	Glu	His	Arg	Arg	Val	His	Thr	Gly	Glu	Arg	
				200					205						210
Leu	Tyr	Gln	Cys	Gly	Lys	Cys	Gly	Lys	Phe	Phe	Ser	Ser	Lys	Ser	
				215					220						225
Asn	Leu	Ile	Arg	His	Gln	Glu	Val	His	Thr	Gly	Ala	Arg	Pro	Tyr	
				230					235						240

Val Cys Ser Glu Cys Gly Lys Glu Phe Ser Arg Lys His Thr Leu	245	250	255
Val Leu His Gln Arg Thr His Thr Gly Glu Arg Pro Tyr Glu Cys	260	265	270
Ser Glu Cys Gly Lys Ala Phe Ser Gln Ser Ser His Leu Asn Val	275	280	285
His Trp Arg Ile His Ser Ser Asp Tyr Glu Cys Ser Arg Cys Gly	290	295	300
Lys Ala Phe Ser Cys Ile Ser Lys Leu Ile Gln His Gln Lys Val	305	310	315
His Ser Gly Glu Lys Pro Tyr Glu Cys Ser Lys Cys Gly Lys Ala	320	325	330
Phe Thr Gln Arg Pro Asn Leu Ile Arg His Trp Lys Val His Thr	335	340	345
Gly Glu Arg Pro Tyr Val Cys Ser Glu Cys Gly Arg Glu Phe Ile	350	355	360
Arg Lys Gln Thr Leu Val Leu His Gln Arg Val His Ala Gly Glu	365	370	375
Lys Leu			

&lt;210&gt; 40

&lt;211&gt; 324

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2765991CD1

&lt;400&gt; 40

Met Asp Phe Pro Lys His Asn Gln Ile Ile Thr Glu Glu Thr Gly	5	10	15
Ser Ala Val Glu Pro Ser Asp Glu Ile Lys Arg Ala Ser Gly Asp	20	25	30
Val Gln Thr Met Lys Ile Ser Ser Val Pro Asn Ser Leu Ser Lys	35	40	45
Arg Asn Val Ser Leu Thr Arg Ser His Ser Val Gly Gly Pro Leu	50	55	60
Gln Asn Ile Asp Phe Thr Gln Arg Pro Phe His Gly Ile Ser Thr	65	70	75
Val Ser Leu Pro Gly Ser Leu Gln Glu Val Val Asp Pro Leu Gly	80	85	90
Lys Arg Pro Asn Pro Pro Pro Val Ser Val Pro Tyr Leu Ser Pro	95	100	105
Leu Val Leu Arg Lys Glu Leu Glu Ser Leu Leu Glu Asn Glu Gly	110	115	120
Asp Gln Val Ile His Thr Ser Ser Phe Ile Asn Gln His Pro Ile	125	130	135
Ile Phe Trp Asn Leu Val Trp Tyr Phe Arg Arg Leu Asp Leu Pro	140	145	150
Ser Asn Leu Pro Gly Leu Ile Leu Thr Ser Glu His Cys Asn Glu	155	160	165
Gly Val Gln Leu Pro Leu Ser Ser Leu Ser Gln Asp Ser Lys Leu	170	175	180
Val Tyr Ile Arg Leu Leu Trp Asp Asn Ile Asn Leu His Gln Glu	185	190	195
Pro Arg Glu Pro Leu Tyr Val Ser Trp Arg Asn Phe Asn Ser Glu	200	205	210
Lys Lys Ser Ser Leu Leu Ser Glu Glu Gln Gln Glu Thr Ser Thr	215	220	225
Leu Val Glu Thr Ile Arg Gln Ser Ile Gln His Asn Asn Val Leu	230	235	240

```

Lys Pro Ile Asn Leu Leu Ser Gln Gln Met Lys Pro Gly Met Lys
245 250 255
Arg Gln Arg Ser Leu Tyr Arg Glu Ile Leu Phe Leu Ser Leu Val
260 265 270
Ser Leu Gly Arg Glu Asn Ile Asp Ile Glu Ala Phe Asp Asn Glu
275 280 285
Tyr Gly Ile Ala Tyr Asn Ser Leu Ser Ser Glu Ile Leu Glu Arg
290 295 300
Leu Gln Lys Ile Asp Ala Pro Pro Ser Ala Ser Val Glu Trp Cys
305 310 315
Arg Lys Cys Phe Gly Ala Pro Leu Ile
320

```

&lt;210&gt; 41

&lt;211&gt; 270

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2775157CD1

&lt;400&gt; 41

```

Met Pro Cys Pro Met Leu Leu Pro Ser Gly Lys Val Ile Asp Gln
1 5 10 15
Ser Thr Leu Glu Lys Cys Asn Arg Ser Glu Ala Thr Trp Gly Arg
20 25 30
Val Pro Ser Asp Pro Phe Thr Gly Val Ala Phe Thr Pro His Ser
35 40 45
Gln Pro Leu Pro His Pro Ser Leu Lys Ala Arg Ile Asp His Phe
50 55 60
Leu Leu Gln His Ser Ile Pro Gly Cys His Leu Leu Gly Arg Ala
65 70 75
Gln Thr Ala Leu Ala Val Ile Pro Ser Ser Ile Val Leu Pro Ser
80 85 90
Gln Lys Arg Lys Ile Glu Gln Ala Glu His Val Pro Asp Ser Asn
95 100 105
Phe Gly Val Asn Ala Ser Cys Phe Ser Ala Thr Ser Pro Leu Val
110 115 120
Leu Pro Thr Thr Ser Glu His Thr Ala Lys Lys Met Lys Ala Thr
125 130 135
Asn Glu Pro Ser Leu Thr His Met Asp Cys Ser Thr Gly Pro Leu
140 145 150
Ser His Glu Gln Lys Leu Ser Gln Ser Leu Glu Ile Ala Leu Ala
155 160 165
Ser Thr Leu Gly Ser Met Pro Ser Phe Thr Ala Arg Leu Thr Arg
170 175 180
Gly Gln Leu Gln His Leu Gly Thr Arg Gly Ser Asn Thr Ser Trp
185 190 195
Arg Pro Gly Thr Gly Ser Glu Gln Pro Gly Ser Ile Leu Gly Pro
200 205 210
Glu Cys Ala Ser Cys Lys Arg Val Phe Ser Pro Tyr Phe Lys Lys
215 220 225
Glu Pro Val Tyr Gln Leu Pro Cys Gly His Leu Leu Cys Arg Pro
230 235 240
Cys Leu Gly Glu Lys Gln Arg Ser Leu Pro Met Thr Cys Thr Ala
245 250 255
Cys Gln Arg Pro Val Ala Ser Gln Asp Val Leu Arg Val His Phe
260 265 270

```

&lt;210&gt; 42

&lt;211&gt; 252

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2918375CD1

&lt;400&gt; 42

```

Met Leu Arg Lys Gly Ile Cys Glu Tyr His Glu Lys Asn Tyr Ala
 1          5          10          15
Ala Ala Leu Glu Thr Phe Thr Glu Gly Gln Lys Leu Asp Ser Ala
          20          25          30
Asp Ala Asn Phe Ser Val Trp Ile Lys Arg Cys Gln Glu Ala Gln
          35          40          45
Asn Gly Ser Glu Ser Glu Val Trp Thr His Gln Ser Lys Ile Lys
          50          55          60
Tyr Asp Trp Tyr Gln Thr Glu Ser Gln Val Val Ile Thr Leu Met
          65          70          75
Ile Lys Asn Val Gln Lys Asn Asp Val Asn Val Glu Phe Ser Glu
          80          85          90
Lys Glu Leu Ser Ala Leu Val Lys Leu Pro Ser Gly Glu Asp Tyr
          95          100          105
Asn Leu Lys Leu Glu Leu Leu His Pro Ile Ile Pro Glu Gln Ser
          110          115          120
Thr Phe Lys Val Leu Ser Thr Lys Ile Glu Ile Lys Leu Lys Lys
          125          130          135
Pro Glu Ala Val Arg Trp Glu Lys Leu Glu Gly Gln Gly Asp Val
          140          145          150
Pro Thr Pro Lys Gln Phe Val Ala Asp Val Lys Asn Leu Tyr Pro
          155          160          165
Ser Ser Ser Pro Tyr Thr Arg Asn Trp Asp Lys Leu Val Gly Glu
          170          175          180
Ile Lys Glu Glu Glu Lys Asn Glu Lys Leu Glu Gly Asp Ala Ala
          185          190          195
Leu Asn Arg Leu Phe Gln Gln Ile Tyr Ser Asp Gly Ser Asp Glu
          200          205          210
Val Lys Arg Ala Met Asn Lys Ser Phe Met Glu Ser Gly Gly Thr
          215          220          225
Val Leu Ser Thr Asn Trp Ser Asp Val Gly Lys Arg Lys Val Glu
          230          235          240
Ile Asn Pro Pro Asp Asp Met Glu Trp Lys Lys Tyr
          245          250

```

&lt;210&gt; 43

&lt;211&gt; 228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 3149729CD1

&lt;400&gt; 43

```

Met Thr Met Gly Asp Lys Lys Ser Pro Thr Arg Pro Lys Arg Gln
 1          5          10          15
Ala Lys Pro Ala Ala Asp Glu Gly Phe Trp Asp Cys Ser Val Cys
          20          25          30
Thr Phe Arg Asn Ser Ala Glu Ala Phe Lys Cys Ser Ile Cys Asp
          35          40          45
Val Arg Lys Gly Thr Ser Thr Arg Lys Pro Arg Ile Asn Ser Gln
          50          55          60

```

```

Leu Val Ala Gln Gln Val Ala Gln Gln Tyr Ala Thr Pro Pro Pro
      65      70      75
Pro Lys Lys Glu Lys Lys Glu Lys Val Glu Lys Gln Asp Lys Glu
      80      85      90
Lys Pro Glu Lys Asp Lys Glu Ile Ser Pro Ser Val Thr Lys Lys
      95     100     105
Asn Thr Asn Lys Lys Thr Lys Pro Lys Ser Asp Ile Leu Lys Asp
     110     115     120
Pro Pro Ser Glu Ala Asn Ser Ile Gln Ser Ala Asn Ala Thr Thr
     125     130     135
Lys Thr Ser Glu Thr Asn His Thr Ser Arg Pro Arg Leu Lys Asn
     140     145     150
Val Asp Arg Ser Thr Ala Gln Gln Leu Ala Val Thr Val Gly Asn
     155     160     165
Val Thr Val Ile Ile Thr Asp Phe Lys Glu Lys Thr Arg Ser Ser
     170     175     180
Ser Thr Ser Ser Ser Thr Val Thr Ser Ser Ala Gly Ser Glu Gln
     185     190     195
Gln Asn Gln Ser Ser Ser Gly Ser Glu Ser Thr Asp Lys Gly Ser
     200     205     210
Ser Arg Ser Ser Thr Pro Lys Gly Asp Met Ser Ala Val Asn Asp
     215     220     225
Glu Ser Phe

```

<210> 44  
 <211> 117  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 3705895CD1

```

<400> 44
Met Ala Ala Ala Ala Ala Ala Gly Ser Gly Thr Pro Arg Glu Glu
  1      5      10      15
Glu Gly Pro Ala Gly Glu Ala Ala Ala Ser Gln Pro Gln Ala Pro
      20      25      30
Thr Ser Val Pro Gly Ala Arg Leu Ser Arg Leu Pro Leu Ala Arg
      35      40      45
Val Lys Ala Leu Val Lys Ala Asp Pro Asp Val Thr Leu Ala Gly
      50      55      60
Gln Glu Ala Ile Phe Ile Leu Ala Arg Ala Ala Glu Leu Phe Val
      65      70      75
Glu Thr Ile Ala Lys Asp Ala Tyr Cys Cys Ala Gln Gln Gly Lys
      80      85      90
Arg Lys Thr Leu Gln Arg Arg Asp Leu Asp Asn Ala Ile Glu Ala
      95     100     105
Val Asp Glu Phe Ala Phe Leu Glu Gly Thr Leu Asp
      110     115

```

<210> 45  
 <211> 252  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 003256CD1

&lt;400&gt; 45

```

Met Thr Pro Lys Leu Gly Arg Gly Val Leu Glu Gly Asp Asp Val
 1      5      10      15
Leu Phe Tyr Asp Glu Ser Pro Pro Pro Arg Pro Lys Leu Ser Ala
 20      25      30
Leu Ala Glu Ala Lys Lys Leu Ala Ala Ile Thr Lys Leu Arg Ala
 35      40      45
Lys Gly Gln Val Leu Thr Lys Thr Asn Pro Asn Ser Ile Lys Lys
 50      55      60
Lys Gln Lys Asp Pro Gln Asp Ile Leu Glu Val Lys Glu Arg Val
 65      70      75
Glu Lys Asn Thr Met Phe Ser Ser Gln Ala Glu Asp Glu Leu Glu
 80      85      90
Pro Ala Arg Lys Lys Arg Arg Glu Gln Leu Ala Tyr Leu Glu Ser
 95      100     105
Glu Glu Phe Gln Lys Ile Leu Lys Ala Lys Ser Lys His Thr Gly
 110     115     120
Ile Leu Lys Glu Ala Glu Ala Glu Met Gln Glu Arg Tyr Phe Glu
 125     130     135
Pro Leu Val Lys Lys Glu Gln Met Glu Glu Lys Met Arg Asn Ile
 140     145     150
Arg Glu Val Lys Cys Arg Val Val Thr Cys Lys Thr Cys Ala Tyr
 155     160     165
Thr His Phe Lys Leu Leu Glu Thr Cys Val Ser Glu Gln His Glu
 170     175     180
Tyr His Trp His Asp Gly Val Lys Arg Phe Phe Lys Cys Pro Cys
 185     190     195
Gly Asn Arg Ser Ile Ser Leu Asp Arg Leu Pro Asn Lys His Cys
 200     205     210
Ser Asn Cys Gly Leu Tyr Lys Trp Glu Arg Asp Gly Met Leu Lys
 215     220     225
Glu Lys Thr Gly Pro Lys Ile Gly Gly Glu Thr Leu Leu Pro Arg
 230     235     240
Gly Glu Glu His Ala Lys Phe Leu Asn Ser Leu Lys
 245     250

```

&lt;210&gt; 46

&lt;211&gt; 530

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 156986CD1

&lt;400&gt; 46

```

Met Ala Lys Gly Glu Gly Ala Glu Ser Gly Ser Ala Ala Gly Leu
 1      5      10      15
Leu Pro Thr Ser Ile Leu Gln Ser Thr Glu Arg Pro Ala Gln Val
 20      25      30
Lys Lys Glu Pro Lys Lys Lys Lys Gln Gln Leu Ser Val Cys Asn
 35      40      45
Lys Leu Cys Tyr Ala Leu Gly Gly Ala Pro Tyr Gln Val Thr Gly
 50      55      60
Cys Ala Leu Gly Phe Phe Leu Gln Ile Tyr Leu Leu Asp Val Ala
 65      70      75
Gln Val Gly Pro Phe Ser Ala Ser Ile Ile Leu Phe Val Gly Arg
 80      85      90
Ala Trp Asp Ala Ile Thr Asp Pro Leu Val Gly Leu Cys Ile Ser
 95      100     105
Lys Ser Pro Trp Thr Cys Leu Gly Arg Leu Met Pro Trp Ile Ile
 110     115     120

```

Phe	Ser	Thr	Pro	Leu	Ala	Val	Ile	Ala	Tyr	Phe	Leu	Ile	Trp	Phe
				125					130					135
Val	Pro	Asp	Phe	Pro	His	Gly	Gln	Thr	Tyr	Trp	Tyr	Leu	Leu	Phe
				140					145					150
Tyr	Cys	Leu	Phe	Glu	Thr	Met	Val	Thr	Cys	Phe	His	Val	Pro	Tyr
				155					160					165
Ser	Ala	Leu	Thr	Met	Phe	Ile	Ser	Thr	Glu	Gln	Thr	Glu	Arg	Asp
				170					175					180
Ser	Ala	Thr	Ala	Tyr	Arg	Met	Thr	Val	Glu	Val	Leu	Gly	Thr	Val
				185					190					195
Leu	Gly	Thr	Ala	Ile	Gln	Gly	Gln	Ile	Val	Gly	Gln	Ala	Asp	Thr
				200					205					210
Pro	Cys	Phe	Gln	Asp	Leu	Asn	Ser	Ser	Thr	Val	Ala	Ser	Gln	Ser
				215					220					225
Ala	Asn	His	Thr	His	Gly	Thr	Thr	Ser	His	Arg	Glu	Thr	Gln	Lys
				230					235					240
Ala	Tyr	Leu	Leu	Ala	Ala	Gly	Val	Ile	Val	Cys	Ile	Tyr	Ile	Ile
				245					250					255
Cys	Ala	Val	Ile	Leu	Ile	Leu	Gly	Val	Arg	Glu	Gln	Arg	Glu	Pro
				260					265					270
Tyr	Glu	Ala	Gln	Gln	Ser	Glu	Pro	Ile	Ala	Tyr	Phe	Arg	Gly	Leu
				275					280					285
Arg	Leu	Val	Met	Ser	His	Gly	Pro	Tyr	Ile	Lys	Leu	Ile	Thr	Gly
				290					295					300
Phe	Leu	Phe	Thr	Ser	Leu	Ala	Phe	Met	Leu	Val	Glu	Gly	Asn	Phe
				305					310					315
Val	Leu	Phe	Cys	Thr	Tyr	Thr	Leu	Gly	Phe	Arg	Asn	Glu	Phe	Gln
				320					325					330
Asn	Leu	Leu	Leu	Ala	Ile	Met	Leu	Ser	Ala	Thr	Leu	Thr	Ile	Pro
				335					340					345
Ile	Trp	Gln	Trp	Phe	Leu	Thr	Arg	Phe	Gly	Lys	Lys	Thr	Ala	Val
				350					355					360
Tyr	Val	Gly	Ile	Ser	Ser	Ala	Val	Pro	Phe	Leu	Ile	Leu	Val	Ala
				365					370					375
Leu	Met	Glu	Ser	Asn	Leu	Ile	Ile	Thr	Tyr	Ala	Val	Ala	Val	Ala
				380					385					390
Ala	Gly	Ile	Ser	Val	Ala	Ala	Ala	Phe	Leu	Leu	Pro	Trp	Ser	Met
				395					400					405
Leu	Pro	Asp	Val	Ile	Asp	Asp	Phe	His	Leu	Lys	Gln	Pro	His	Phe
				410					415					420
His	Gly	Thr	Glu	Pro	Ile	Phe	Phe	Ser	Phe	Tyr	Val	Phe	Phe	Thr
				425					430					435
Lys	Phe	Ala	Ser	Gly	Val	Ser	Leu	Gly	Ile	Ser	Thr	Leu	Ser	Leu
				440					445					450
Asp	Phe	Ala	Gly	Tyr	Gln	Thr	Arg	Gly	Cys	Ser	Gln	Pro	Glu	Arg
				455					460					465
Val	Lys	Phe	Thr	Leu	Asn	Met	Leu	Val	Thr	Met	Ala	Pro	Ile	Val
				470					475					480
Leu	Ile	Leu	Leu	Gly	Leu	Leu	Leu	Phe	Lys	Met	Tyr	Pro	Ile	Asp
				485					490					495
Glu	Glu	Arg	Arg	Arg	Gln	Asn	Lys	Lys	Ala	Leu	Gln	Ala	Leu	Arg
				500					505					510
Asp	Glu	Ala	Ser	Ser	Ser	Gly	Cys	Ser	Glu	Thr	Asp	Ser	Thr	Glu
				515					520					525
Leu	Ala	Ser	Ile	Leu										
				530										

&lt;210&gt; 47

&lt;211&gt; 355

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 319415CD1

&lt;400&gt; 47

Met	Gly	Cys	Val	Phe	Gln	Ser	Thr	Glu	Asp	Lys	Cys	Ile	Phe	Lys
1				5					10					15
Ile	Asp	Trp	Thr	Leu	Ser	Pro	Gly	Glu	His	Ala	Lys	Asp	Glu	Tyr
				20					25					30
Val	Leu	Tyr	Tyr	Tyr	Ser	Asn	Leu	Ser	Val	Pro	Ile	Gly	Arg	Phe
				35					40					45
Gln	Asn	Arg	Val	His	Leu	Met	Gly	Asp	Ile	Leu	Cys	Asn	Asp	Gly
				50					55					60
Ser	Leu	Leu	Leu	Gln	Asp	Val	Gln	Glu	Ala	Asp	Gln	Gly	Thr	Tyr
				65					70					75
Ile	Cys	Glu	Ile	Arg	Leu	Lys	Gly	Glu	Ser	Gln	Val	Phe	Lys	Lys
				80					85					90
Ala	Val	Val	Leu	His	Val	Leu	Pro	Glu	Glu	Pro	Lys	Glu	Leu	Met
				95					100					105
Val	His	Val	Gly	Gly	Leu	Ile	Gln	Met	Gly	Cys	Val	Phe	Gln	Ser
				110					115					120
Thr	Glu	Val	Lys	His	Val	Thr	Lys	Val	Glu	Trp	Ile	Phe	Ser	Gly
				125					130					135
Arg	Arg	Ala	Lys	Glu	Glu	Ile	Val	Phe	Arg	Tyr	Tyr	His	Lys	Leu
				140					145					150
Arg	Met	Ser	Val	Glu	Tyr	Ser	Gln	Ser	Trp	Gly	His	Phe	Gln	Asn
				155					160					165
Arg	Val	Asn	Leu	Val	Gly	Asp	Ile	Phe	Arg	Asn	Asp	Gly	Ser	Ile
				170					175					180
Met	Leu	Gln	Gly	Val	Arg	Glu	Ser	Asp	Gly	Gly	Asn	Tyr	Thr	Cys
				185					190					195
Ser	Ile	His	Leu	Gly	Asn	Leu	Val	Phe	Lys	Lys	Thr	Ile	Val	Leu
				200					205					210
His	Val	Ser	Pro	Glu	Glu	Pro	Arg	Thr	Leu	Val	Thr	Pro	Ala	Ala
				215					220					225
Leu	Arg	Pro	Leu	Val	Leu	Gly	Gly	Asn	Gln	Leu	Val	Ile	Ile	Val
				230					235					240
Gly	Ile	Val	Cys	Ala	Thr	Ile	Leu	Leu	Leu	Pro	Val	Leu	Ile	Leu
				245					250					255
Ile	Val	Lys	Lys	Thr	Cys	Gly	Asn	Lys	Ser	Ser	Val	Asn	Ser	Thr
				260					265					270
Val	Leu	Val	Lys	Asn	Thr	Lys	Lys	Thr	Asn	Pro	Glu	Ile	Lys	Glu
				275					280					285
Lys	Pro	Cys	His	Phe	Glu	Arg	Cys	Glu	Gly	Glu	Lys	His	Ile	Tyr
				290					295					300
Ser	Pro	Ile	Ile	Val	Arg	Glu	Val	Ile	Glu	Glu	Glu	Glu	Pro	Ser
				305					310					315
Glu	Lys	Ser	Glu	Ala	Thr	Tyr	Met	Thr	Met	His	Pro	Val	Trp	Pro
				320					325					330
Ser	Leu	Arg	Ser	Asp	Arg	Asn	Asn	Ser	Leu	Glu	Lys	Lys	Ser	Gly
				335					340					345
Gly	Gly	Met	Pro	Lys	Thr	Gln	Gln	Ala	Phe					
				350					355					

&lt;210&gt; 48

&lt;211&gt; 136

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 635581CD1

&lt;400&gt; 48

Met	Val	Gly	Gln	Thr	Glu	Asp	Asp	Thr	Ala	Gln	Gln	Leu	Val	Pro
1				5					10					15
Thr	Cys	Gly	Met	Lys	Gly	Val	Gly	Glu	Arg	Ile	Val	Glu	Tyr	Val
			20					25						30
Ser	Asn	Ile	Pro	Ala	Leu	Gln	Arg	Ala	Thr	Pro	Lys	Gly	Leu	Ala
			35					40						45
Ser	Val	Ser	Pro	Asp	Leu	Glu	His	Arg	Gln	Glu	Trp	Thr	Tyr	Ser
			50					55						60
Lys	Ser	Pro	Leu	Met	Gly	Lys	Gly	Thr	Arg	Leu	Glu	Ala	Ser	Glu
			65					70						75
Asn	Lys	Arg	Ala	Gly	Trp	Leu	Ala	Ala	Ala	Pro	Glu	Asn	Leu	Lys
			80					85						90
Tyr	His	Arg	Gln	Ile	Ala	Gln	Gly	Ala	Lys	Asp	Tyr	Glu	Ile	Leu
			95					100						105
Lys	Lys	Glu	Thr	Asn	Lys	Phe	Ile	Leu	Arg	Ile	Tyr	Thr	His	Trp
			110					115						120
Ser	Arg	Arg	Ser	Ile	Leu	Arg	Lys	Gly	Ser	Lys	Gly	Met	Gln	Asn
			125					130						135

Leu

&lt;210&gt; 49

&lt;211&gt; 230

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;223&gt; Incyte clone 921803CD1

&lt;400&gt; 49

Met	Lys	Leu	Ile	Val	Gly	Ile	Gly	Gly	Met	Thr	Asn	Gly	Gly	Lys
1				5					10					15
Thr	Thr	Leu	Thr	Asn	Ser	Leu	Leu	Arg	Ala	Leu	Pro	Asn	Cys	Cys
			20					25						30
Val	Ile	His	Gln	Asp	Asp	Phe	Phe	Lys	Pro	Gln	Asp	Gln	Ile	Ala
			35					40						45
Val	Gly	Glu	Asp	Gly	Phe	Lys	Gln	Trp	Asp	Val	Leu	Glu	Ser	Leu
			50					55						60
Asp	Met	Glu	Ala	Met	Leu	Asp	Thr	Val	Gln	Ala	Trp	Leu	Ser	Ser
			65					70						75
Pro	Gln	Lys	Phe	Ala	Arg	Ala	His	Gly	Val	Ser	Val	Gln	Pro	Glu
			80					85						90
Ala	Ser	Asp	Thr	His	Ile	Leu	Leu	Leu	Glu	Gly	Phe	Leu	Leu	Tyr
			95					100						105
Ser	Tyr	Lys	Pro	Leu	Val	Asp	Leu	Tyr	Ser	Arg	Arg	Tyr	Phe	Leu
			110					115						120
Thr	Val	Pro	Tyr	Glu	Glu	Cys	Lys	Trp	Arg	Arg	Ser	Thr	Arg	Asn
			125					130						135
Tyr	Thr	Val	Pro	Asp	Pro	Pro	Gly	Leu	Phe	Asp	Gly	His	Val	Trp
			140					145						150
Pro	Met	Tyr	Gln	Lys	Tyr	Arg	Gln	Glu	Met	Glu	Ala	Asn	Gly	Val
			155					160						165
Glu	Val	Val	Tyr	Leu	Asp	Gly	Met	Lys	Ser	Arg	Glu	Glu	Leu	Phe
			170					175						180
Arg	Glu	Val	Leu	Glu	Asp	Ile	Gln	Asn	Ser	Leu	Leu	Asn	Arg	Ser
			185					190						195
Gln	Glu	Ser	Ala	Pro	Ser	Pro	Ala	Arg	Pro	Ala	Arg	Thr	Gln	Gly
			200					205						210

Pro Gly Arg Gly Cys Gly His Arg Thr Ala Arg Pro Ala Ala Ser  
 215 220 225  
 Gln Gln Asp Ser Met  
 230

<210> 50  
 <211> 70  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1250492CD1

<400> 50  
 Met Thr Ile Lys Leu Arg Pro Leu Pro Phe Phe Lys Pro Lys Ser  
 1 5 10 15  
 Gly Asn Gln Glu Gln Gln Leu His Gly Leu Leu Ala Pro Asp Gln  
 20 25 30  
 Pro Gly Ser Gly Asp Ile Val Ser Leu Phe Gly Asn Cys Arg Pro  
 35 40 45  
 Gln Gly Val Gly Leu Ser His Phe Leu Val Leu Pro Thr Phe Pro  
 50 55 60  
 Ile Arg Ala Ser Ser Arg Gly Gln Val Cys  
 65 70

<210> 51  
 <211> 169  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1427838CD1

<400> 51  
 Met Leu Ala Phe Ser Glu Met Pro Lys Pro Pro Asp Tyr Ser Glu  
 1 5 10 15  
 Leu Ser Asp Ser Leu Thr Leu Ala Val Gly Thr Gly Arg Phe Ser  
 20 25 30  
 Gly Pro Leu His Arg Ala Trp Arg Met Met Asn Phe Arg Gln Arg  
 35 40 45  
 Met Gly Trp Ile Gly Val Gly Leu Tyr Leu Leu Ala Ser Ala Ala  
 50 55 60  
 Ala Phe Tyr Tyr Val Phe Glu Ile Ser Glu Thr Tyr Asn Arg Leu  
 65 70 75  
 Ala Leu Glu His Ile Gln Gln His Pro Glu Glu Pro Leu Glu Gly  
 80 85 90  
 Thr Thr Trp Thr His Ser Leu Lys Ala Gln Leu Leu Ser Leu Pro  
 95 100 105  
 Phe Trp Val Trp Thr Val Ile Phe Leu Val Pro Tyr Leu Gln Met  
 110 115 120  
 Phe Leu Phe Leu Tyr Ser Cys Thr Arg Ala Asp Pro Lys Thr Val  
 125 130 135  
 Gly Tyr Cys Ile Ile Pro Ile Cys Leu Ala Val Ile Cys Asn Arg  
 140 145 150  
 His Gln Ala Phe Val Lys Ala Ser Asn Gln Ile Ser Arg Leu Gln  
 155 160 165  
 Leu Ile Asp Thr

<210> 52  
 <211> 359  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1448258CD1

<400> 52

Met	Gly	Pro	Thr	Lys	Phe	Thr	Gln	Thr	Asn	Ile	Gly	Ile	Ile	Glu
1				5					10					15
Asn	Lys	Leu	Leu	Glu	Ala	Pro	Asp	Val	Leu	Cys	Leu	Arg	Leu	Ser
				20					25					30
Thr	Glu	Gln	Cys	Gln	Ala	His	Glu	Glu	Lys	Gly	Ile	Glu	Glu	Leu
				35					40					45
Ser	Asp	Pro	Ser	Gly	Pro	Lys	Ser	Tyr	Ser	Ile	Thr	Glu	Lys	His
				50					55					60
Tyr	Ala	Gln	Glu	Asp	Pro	Arg	Met	Leu	Phe	Val	Ala	Ala	Val	Asp
				65					70					75
His	Ser	Ser	Ser	Gly	Asp	Met	Ser	Leu	Leu	Pro	Ser	Ser	Asp	Pro
				80					85					90
Lys	Phe	Gln	Gly	Leu	Gly	Val	Val	Glu	Ser	Ala	Val	Thr	Ala	Asn
				95					100					105
Asn	Thr	Glu	Glu	Ser	Leu	Phe	Arg	Ile	Cys	Ser	Pro	Leu	Ser	Gly
				110					115					120
Ala	Asn	Glu	Tyr	Ile	Ala	Ser	Thr	Asp	Thr	Leu	Lys	Thr	Glu	Glu
				125					130					135
Val	Leu	Leu	Phe	Thr	Asp	Gln	Thr	Asp	Asp	Leu	Ala	Lys	Glu	Glu
				140					145					150
Pro	Thr	Ser	Leu	Phe	Gln	Arg	Asp	Ser	Glu	Thr	Lys	Gly	Glu	Ser
				155					160					165
Gly	Leu	Val	Leu	Glu	Gly	Asp	Lys	Glu	Ile	His	Gln	Ile	Phe	Glu
				170					175					180
Asp	Leu	Asp	Lys	Lys	Leu	Ala	Leu	Ala	Ser	Arg	Phe	Tyr	Ile	Pro
				185					190					195
Glu	Gly	Cys	Ile	Gln	Arg	Trp	Ala	Ala	Glu	Met	Val	Val	Ala	Leu
				200					205					210
Asp	Ala	Leu	His	Arg	Glu	Gly	Ile	Val	Cys	Arg	Asp	Leu	Asn	Pro
				215					220					225
Asn	Asn	Ile	Leu	Leu	Asn	Asp	Arg	Gly	His	Ile	Gln	Leu	Thr	Tyr
				230					235					240
Phe	Ser	Arg	Trp	Ser	Glu	Val	Glu	Asp	Ser	Cys	Asp	Ser	Asp	Ala
				245					250					255
Ile	Glu	Arg	Met	Tyr	Cys	Ala	Pro	Glu	Val	Gly	Ala	Ile	Thr	Glu
				260					265					270
Glu	Thr	Glu	Ala	Cys	Asp	Trp	Trp	Ser	Leu	Gly	Ala	Val	Leu	Phe
				275					280					285
Glu	Leu	Leu	Thr	Gly	Lys	Thr	Leu	Val	Glu	Cys	His	Pro	Ala	Gly
				290					295					300
Ile	Asn	Thr	His	Thr	Thr	Leu	Asn	Met	Pro	Glu	Cys	Val	Ser	Glu
				305					310					315
Glu	Ala	Arg	Ser	Leu	Ile	Gln	Gln	Leu	Leu	Gln	Phe	Asn	Pro	Leu
				320					325					330
Glu	Arg	Leu	Gly	Ala	Gly	Val	Ala	Gly	Val	Glu	Asp	Ile	Lys	Ser
				335					340					345
His	Pro	Phe	Phe	Thr	Pro	Val	Asp	Trp	Ala	Glu	Leu	Met	Arg	
				350					355					

<210> 53  
 <211> 545

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1645941CD1

&lt;400&gt; 53

Met	Ser	Arg	Lys	Gln	Asn	Gln	Lys	Asp	Ser	Ser	Gly	Phe	Ile	Phe
1				5					10					15
Asp	Leu	Gln	Ser	Asn	Thr	Val	Leu	Ala	Gln	Gly	Gly	Ala	Phe	Glu
				20					25					30
Asn	Met	Lys	Glu	Lys	Ile	Asn	Ala	Val	Arg	Ala	Ile	Val	Pro	Asn
				35					40					45
Lys	Ser	Asn	Asn	Glu	Ile	Ile	Leu	Val	Leu	Gln	His	Phe	Asp	Asn
				50					55					60
Cys	Val	Asp	Lys	Thr	Val	Gln	Ala	Phe	Met	Glu	Gly	Ser	Ala	Ser
				65					70					75
Glu	Val	Leu	Lys	Glu	Trp	Thr	Val	Thr	Gly	Lys	Lys	Lys	Asn	Lys
				80					85					90
Lys	Lys	Lys	Asn	Lys	Pro	Lys	Pro	Ala	Ala	Glu	Pro	Ser	Asn	Gly
				95					100					105
Ile	Pro	Asp	Ser	Ser	Lys	Ser	Val	Ser	Ile	Gln	Glu	Glu	Gln	Ser
				110					115					120
Ala	Pro	Ser	Ser	Glu	Lys	Gly	Gly	Met	Asn	Gly	Tyr	His	Val	Asn
				125					130					135
Gly	Ala	Ile	Asn	Asp	Thr	Glu	Ser	Val	Asp	Ser	Leu	Ser	Glu	Gly
				140					145					150
Leu	Glu	Thr	Leu	Ser	Ile	Asp	Ala	Arg	Glu	Leu	Glu	Asp	Pro	Glu
				155					160					165
Ser	Ala	Met	Leu	Asp	Thr	Leu	Asp	Arg	Thr	Gly	Ser	Met	Leu	Gln
				170					175					180
Asn	Gly	Val	Ser	Asp	Phe	Glu	Thr	Lys	Ser	Leu	Thr	Met	His	Ser
				185					190					195
Ile	His	Asn	Ser	Gln	Gln	Pro	Arg	Asn	Ala	Ala	Lys	Ser	Leu	Ser
				200					205					210
Arg	Pro	Thr	Thr	Glu	Thr	Gln	Phe	Ser	Asn	Met	Gly	Met	Glu	Asp
				215					220					225
Val	Pro	Leu	Ala	Thr	Ser	Lys	Lys	Leu	Ser	Ser	Asn	Ile	Glu	Lys
				230					235					240
Ser	Val	Lys	Asp	Leu	Gln	Arg	Cys	Thr	Val	Ser	Leu	Ala	Arg	Tyr
				245					250					255
Arg	Val	Val	Val	Lys	Glu	Glu	Met	Asp	Ala	Ser	Ile	Lys	Lys	Met
				260					265					270
Lys	Gln	Ala	Phe	Ala	Glu	Leu	Glu	Ser	Cys	Leu	Met	Asp	Arg	Glu
				275					280					285
Val	Ala	Leu	Leu	Ala	Glu	Met	Asp	Lys	Val	Lys	Ala	Glu	Ala	Met
				290					295					300
Glu	Ile	Leu	Leu	Ser	Arg	Gln	Lys	Lys	Ala	Glu	Leu	Leu	Lys	Lys
				305					310					315
Met	Thr	His	Val	Ala	Val	Gln	Met	Ser	Glu	Gln	Gln	Leu	Val	Glu
				320					325					330
Leu	Arg	Ala	Asp	Ile	Lys	His	Phe	Val	Ser	Glu	Arg	Lys	Tyr	Asp
				335					340					345
Glu	Asp	Leu	Gly	Arg	Val	Ala	Arg	Phe	Thr	Cys	Asp	Val	Glu	Thr
				350					355					360
Leu	Lys	Lys	Ser	Ile	Asp	Ser	Phe	Gly	Gln	Val	Ser	His	Pro	Lys
				365					370					375
Asn	Ser	Tyr	Ser	Thr	Arg	Ser	Arg	Cys	Ser	Ser	Val	Thr	Ser	Val
				380					385					390
Ser	Leu	Ser	Ser	Pro	Ser	Asp	Ala	Ser	Ala	Ala	Ser	Ser	Ser	Thr
				395					400					405
Cys	Ala	Ser	Pro	Pro	Ser	Leu	Thr	Ser	Ala	Asn	Lys	Lys	Asn	Phe
				410					415					420

Ala	Pro	Gly	Glu	Thr	Pro	Ala	Ala	Ile	Ala	Asn	Ser	Ser	Gly	Gln	
				425					430					435	
Pro	Tyr	Gln	Pro	Leu	Arg	Glu	Val	Leu	Pro	Gly	Asn	Arg	Arg	Gly	
				440					445					450	
Gly	Gln	Gly	Tyr	Arg	Pro	Gln	Gly	Gln	Lys	Ser	Asn	Asp	Pro	Met	
				455					460					465	
Asn	Gln	Gly	Arg	His	Asp	Ser	Met	Gly	Arg	Tyr	Arg	Asn	Ser	Ser	
				470					475					480	
Trp	Tyr	Ser	Ser	Gly	Ser	Arg	Tyr	Gln	Ser	Ala	Pro	Ser	Gln	Ala	
				485					490					495	
Pro	Gly	Asn	Thr	Ile	Glu	Arg	Gly	Gln	Thr	His	Ser	Ala	Gly	Thr	
				500					505					510	
Asn	Gly	Thr	Gly	Val	Ser	Met	Glu	Pro	Ser	Pro	Pro	Thr	Pro	Ser	
				515					520					525	
Phe	Lys	Lys	Gly	Leu	Pro	Gln	Arg	Lys	Pro	Arg	Thr	Ser	Gln	Thr	
				530					535					540	
Glu	Ala	Val	Asn	Ser											
				545											

<210> 54  
 <211> 99  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1646005CD1

<400>	54														
Met	Asn	Trp	Val	Ala	Val	Leu	Cys	Pro	Leu	Gly	Ile	Val	Trp	Met	
1				5					10					15	
Val	Gly	Asp	Gln	Pro	Pro	Gln	Val	Leu	Ser	Gln	Ala	Ser	Ser	Leu	
				20					25					30	
Ala	Val	Tyr	Leu	Arg	Ala	Ala	Pro	Tyr	Pro	Asp	Val	Thr	Ala	Lys	
				35					40					45	
Lys	Leu	Arg	His	Asp	Thr	Asn	Cys	Gly	Phe	Pro	Arg	Gln	Gln	Arg	
				50					55					60	
Met	Ala	Arg	Gly	His	Glu	Gly	Arg	Ala	Pro	Leu	Leu	Asp	Arg	Pro	
				65					70					75	
Thr	Leu	Lys	Ser	Arg	Tyr	Leu	Arg	Ala	Asn	His	Lys	Ile	Asn	Thr	
				80					85					90	
Phe	Glu	Glu	Ile	Thr	Ala	Met	Pro	Ser							
				95											

<210> 55  
 <211> 565  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1686561CD1

<400>	55														
Met	Asn	Arg	Ser	Ile	Pro	Val	Glu	Val	Asp	Glu	Ser	Glu	Pro	Tyr	
1				5					10					15	
Pro	Ser	Gln	Leu	Leu	Lys	Pro	Ile	Pro	Glu	Tyr	Ser	Pro	Glu	Glu	
				20					25					30	
Glu	Ser	Glu	Pro	Pro	Ala	Pro	Asn	Ile	Arg	Asn	Met	Ala	Pro	Asn	
				35					40					45	
Ser	Leu	Ser	Ala	Pro	Thr	Met	Leu	His	Asn	Ser	Ser	Gly	Asp	Phe	
				50					55					60	

Ser	Gln	Ala	His	Ser	Thr	Leu	Lys	Leu	Ala	Asn	His	Gln	Arg	Pro
				65					70					75
Val	Ser	Arg	Gln	Val	Thr	Cys	Leu	Arg	Thr	Gln	Val	Leu	Glu	Asp
				80					85					90
Ser	Glu	Asp	Ser	Phe	Cys	Arg	Arg	His	Pro	Gly	Leu	Gly	Lys	Ala
				95					100					105
Phe	Pro	Ser	Gly	Cys	Ser	Ala	Val	Ser	Glu	Pro	Ala	Ser	Glu	Ser
				110					115					120
Val	Val	Gly	Ala	Leu	Pro	Ala	Glu	His	Gln	Phe	Ser	Phe	Met	Glu
				125					130					135
Lys	Arg	Asn	Gln	Trp	Leu	Val	Ser	Gln	Leu	Ser	Ala	Ala	Ser	Pro
				140					145					150
Asp	Thr	Gly	His	Asp	Ser	Asp	Lys	Ser	Asp	Gln	Ser	Leu	Pro	Asn
				155					160					165
Ala	Ser	Ala	Asp	Ser	Leu	Gly	Gly	Ser	Gln	Glu	Met	Val	Gln	Arg
				170					175					180
Pro	Gln	Pro	His	Arg	Asn	Arg	Ala	Gly	Leu	Asp	Leu	Pro	Thr	Ile
				185					190					195
Asp	Thr	Gly	Tyr	Asp	Ser	Gln	Pro	Gln	Asp	Val	Leu	Gly	Ile	Arg
				200					205					210
Gln	Leu	Glu	Arg	Pro	Leu	Pro	Leu	Thr	Ser	Val	Cys	Tyr	Pro	Gln
				215					220					225
Asp	Leu	Pro	Arg	Pro	Leu	Arg	Ser	Arg	Glu	Phe	Pro	Gln	Phe	Glu
				230					235					240
Pro	Gln	Arg	Tyr	Pro	Ala	Cys	Ala	Gln	Met	Leu	Pro	Pro	Asn	Leu
				245					250					255
Ser	Pro	His	Ala	Pro	Trp	Asn	Tyr	His	Tyr	His	Cys	Pro	Gly	Ser
				260					265					270
Pro	Asp	His	Gln	Val	Pro	Tyr	Gly	His	Asp	Tyr	Pro	Arg	Ala	Ala
				275					280					285
Tyr	Gln	Gln	Val	Ile	Gln	Pro	Ala	Leu	Pro	Gly	Gln	Pro	Leu	Pro
				290					295					300
Gly	Ala	Ser	Val	Arg	Gly	Leu	His	Pro	Val	Gln	Lys	Val	Ile	Leu
				305					310					315
Asn	Tyr	Pro	Ser	Pro	Trp	Asp	Gln	Glu	Glu	Arg	Pro	Ala	Gln	Arg
				320					325					330
Asp	Cys	Ser	Phe	Pro	Gly	Leu	Pro	Arg	His	Gln	Asp	Gln	Pro	His
				335					340					345
His	Gln	Pro	Pro	Asn	Arg	Ala	Gly	Ala	Pro	Gly	Glu	Ser	Leu	Glu
				350					355					360
Cys	Pro	Ala	Glu	Leu	Arg	Pro	Gln	Val	Pro	Gln	Pro	Pro	Ser	Pro
				365					370					375
Ala	Ala	Val	Pro	Arg	Pro	Pro	Ser	Asn	Pro	Pro	Ala	Arg	Gly	Thr
				380					385					390
Leu	Lys	Thr	Ser	Asn	Leu	Pro	Glu	Glu	Leu	Arg	Lys	Val	Phe	Ile
				395					400					405
Thr	Tyr	Ser	Met	Asp	Thr	Ala	Met	Glu	Val	Val	Lys	Phe	Val	Asn
				410					415					420
Phe	Leu	Leu	Val	Asn	Gly	Phe	Gln	Thr	Ala	Ile	Asp	Ile	Phe	Glu
				425					430					435
Asp	Arg	Ile	Arg	Gly	Ile	Asp	Ile	Ile	Lys	Trp	Met	Glu	Arg	Tyr
				440					445					450
Leu	Arg	Asp	Lys	Thr	Val	Met	Ile	Ile	Val	Ala	Ile	Ser	Pro	Lys
				455					460					465
Tyr	Lys	Gln	Asp	Val	Glu	Gly	Ala	Glu	Ser	Gln	Leu	Asp	Glu	Asp
				470					475					480
Glu	His	Gly	Leu	His	Thr	Lys	Tyr	Ile	His	Arg	Met	Met	Gln	Ile
				485					490					495
Glu	Phe	Ile	Lys	Gln	Gly	Ser	Met	Asn	Phe	Arg	Phe	Ile	Pro	Val
				500					505					510
Leu	Phe	Pro	Asn	Ala	Lys	Lys	Glu	His	Val	Pro	Thr	Trp	Leu	Gln
				515					520					525
Asn	Thr	His	Val	Tyr	Ser	Trp	Pro	Lys	Asn	Lys	Lys	Asn	Ile	Leu
				530					535					540

Leu Arg Leu Leu Arg Glu Glu Glu Tyr Val Ala Pro Pro Arg Gly  
 545 550 555  
 Pro Leu Pro Thr Leu Gln Val Val Pro Leu  
 560 565

<210> 56  
 <211> 197  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1821233CD1

<400> 56  
 Met Thr Pro Thr Ser Ser Phe Val Ser Pro Pro Pro Pro Thr Ala  
 1 5 10 15  
 Ser Pro His Ser Asn Arg Thr Thr Pro Pro Glu Ala Ala Gln Asn  
 20 25 30  
 Gly Gln Ser Pro Met Ala Ala Leu Ile Leu Val Ala Asp Asn Ala  
 35 40 45  
 Gly Gly Ser His Ala Ser Lys Asp Ala Asn Gln Val His Ser Thr  
 50 55 60  
 Thr Arg Arg Asn Ser Asn Ser Pro Pro Ser Pro Ser Ser Met Asn  
 65 70 75  
 Gln Arg Arg Leu Gly Pro Arg Glu Val Gly Gly Gln Gly Ala Gly  
 80 85 90  
 Asn Thr Gly Gly Leu Glu Pro Val His Pro Ala Ser Leu Pro Asp  
 95 100 105  
 Ser Ser Leu Ala Thr Ser Ala Pro Leu Cys Cys Thr Leu Cys His  
 110 115 120  
 Glu Arg Leu Glu Asp Thr His Phe Val Gln Cys Pro Ser Val Pro  
 125 130 135  
 Ser His Lys Phe Cys Phe Pro Cys Ser Arg Gln Ser Ile Lys Gln  
 140 145 150  
 Gln Gly Ala Ser Gly Glu Val Tyr Cys Pro Ser Gly Glu Lys Cys  
 155 160 165  
 Pro Leu Val Gly Ser Asn Val Pro Trp Ala Phe Met Gln Gly Glu  
 170 175 180  
 Ile Ala Thr Ile Leu Ala Gly Asp Val Lys Val Lys Lys Glu Arg  
 185 190 195  
 Asp Ser

<210> 57  
 <211> 321  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1877278CD1

<400> 57  
 Met Lys Glu Asp Cys Leu Pro Ser Ser His Val Pro Ile Ser Asp  
 1 5 10 15  
 Ser Lys Ser Ile Gln Lys Ser Glu Leu Leu Gly Leu Leu Lys Thr  
 20 25 30  
 Tyr Asn Cys Tyr His Glu Gly Lys Ser Phe Gln Leu Arg His Arg  
 35 40 45



Glu	Glu	Glu	Gly	Thr	Leu	Ile	Ile	Glu	Gly	Leu	Leu	Asn	Ile	Ala	
				50					55					60	
Trp	Gly	Leu	Arg	Arg	Pro	Ile	Arg	Leu	Gln	Met	Gln	Asp	Asp	Arg	
				65					70					75	
Glu	Gln	Val	His	Leu	Pro	Ser	Thr	Ser	Trp	Met	Pro	Arg	Arg	Pro	
				80					85					90	
Ser	Cys	Pro	Leu	Lys	Glu	Pro	Ser	Pro	Gln	Asn	Gly	Asn	Ile	Thr	
				95					100					105	
Ala	Gln	Gly	Pro	Ser	Ile	Gln	Pro	Val	His	Lys	Ala	Glu	Ser	Ser	
				110					115					120	
Thr	Asp	Ser	Ser	Gly	Pro	Leu	Glu	Glu	Ala	Glu	Glu	Ala	Pro	Gln	
				125					130					135	
Leu	Met	Arg	Thr	Lys	Ser	Asp	Ala	Ser	Cys	Met	Ser	Gln	Arg	Arg	
				140					145					150	
Pro	Lys	Cys	Arg	Ala	Pro	Gly	Glu	Ala	Gln	Arg	Ile	Arg	Arg	His	
				155					160					165	
Arg	Phe	Ser	Ile	Asn	Gly	His	Phe	Tyr	Asn	His	Lys	Thr	Ser	Val	
				170					175					180	
Phe	Thr	Pro	Ala	Tyr	Gly	Ser	Val	Thr	Asn	Val	Arg	Val	Asn	Ser	
				185					190					195	
Thr	Met	Thr	Thr	Leu	Gln	Val	Leu	Thr	Leu	Leu	Leu	Asn	Lys	Phe	
				200					205					210	
Arg	Val	Glu	Asp	Gly	Pro	Ser	Glu	Phe	Ala	Leu	Tyr	Ile	Val	His	
				215					220					225	
Glu	Ser	Gly	Glu	Arg	Thr	Lys	Leu	Lys	Asp	Cys	Glu	Tyr	Pro	Leu	
				230					235					240	
Ile	Ser	Arg	Ile	Leu	His	Gly	Pro	Cys	Glu	Lys	Ile	Ala	Arg	Ile	
				245					250					255	
Phe	Leu	Met	Glu	Ala	Asp	Leu	Gly	Val	Glu	Val	Pro	His	Glu	Val	
				260					265					270	
Ala	Gln	Tyr	Ile	Lys	Phe	Glu	Met	Pro	Val	Leu	Asp	Ser	Phe	Val	
				275					280					285	
Glu	Lys	Leu	Lys	Glu	Glu	Glu	Glu	Arg	Glu	Ile	Ile	Lys	Leu	Thr	
				290					295					300	
Met	Lys	Phe	Gln	Ala	Leu	Arg	Leu	Thr	Met	Leu	Gln	Arg	Leu	Glu	
				305					310					315	
Gln	Leu	Val	Glu	Ala	Lys										
				320											

&lt;210&gt; 58

&lt;211&gt; 356

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1880692CD1

&lt;400&gt; 58

Met	Glu	Trp	Leu	Lys	Ser	Thr	Asp	Tyr	Gly	Lys	Tyr	Glu	Gly	Leu	
1				5					10					15	
Thr	Lys	Asn	Tyr	Met	Asp	Tyr	Leu	Ser	Arg	Leu	Tyr	Glu	Arg	Glu	
				20					25					30	
Ile	Lys	Asp	Phe	Phe	Glu	Val	Ala	Lys	Ile	Lys	Met	Thr	Gly	Thr	
				35					40					45	
Thr	Lys	Glu	Ser	Lys	Lys	Phe	Gly	Leu	His	Gly	Ser	Ser	Gly	Lys	
				50					55					60	
Leu	Thr	Gly	Ser	Thr	Ser	Ser	Leu	Asn	Lys	Leu	Ser	Val	Gln	Ser	
				65					70					75	
Ser	Gly	Asn	Arg	Arg	Ser	Gln	Ser	Ser	Ser	Leu	Leu	Asp	Met	Gly	
				80					85					90	
Asn	Met	Ser	Ala	Ser	Asp	Leu	Asp	Val	Ala	Asp	Arg	Thr	Lys	Phe	
				95					100					105	

Asp	Lys	Ile	Phe	Glu	Gln	Val	Leu	Ser	Glu	Leu	Glu	Pro	Leu	Cys
				110					115					120
Leu	Ala	Glu	Gln	Asp	Phe	Ile	Ser	Lys	Phe	Phe	Lys	Leu	Gln	Gln
				125					130					135
His	Gln	Ser	Met	Pro	Gly	Thr	Met	Ala	Glu	Ala	Glu	Asp	Leu	Asp
				140					145					150
Gly	Gly	Thr	Leu	Ser	Arg	Gln	His	Asn	Cys	Gly	Thr	Pro	Leu	Pro
				155					160					165
Val	Ser	Ser	Glu	Lys	Asp	Met	Ile	Arg	Gln	Met	Met	Ile	Lys	Ile
				170					175					180
Phe	Arg	Cys	Ile	Glu	Pro	Glu	Leu	Asn	Asn	Leu	Ile	Ala	Leu	Gly
				185					190					195
Asp	Lys	Ile	Asp	Ser	Phe	Asn	Ser	Leu	Tyr	Met	Leu	Val	Lys	Met
				200					205					210
Ser	His	His	Val	Trp	Thr	Ala	Gln	Asn	Val	Asp	Pro	Ala	Ser	Phe
				215					220					225
Leu	Ser	Thr	Thr	Leu	Gly	Asn	Val	Leu	Val	Thr	Val	Lys	Arg	Asn
				230					235					240
Phe	Asp	Lys	Cys	Ile	Ser	Asn	Gln	Ile	Arg	Gln	Met	Glu	Glu	Val
				245					250					255
Lys	Ile	Ser	Lys	Lys	Ser	Lys	Val	Gly	Ile	Leu	Pro	Phe	Val	Ala
				260					265					270
Glu	Phe	Glu	Glu	Phe	Ala	Gly	Leu	Ala	Glu	Ser	Ile	Phe	Lys	Asn
				275					280					285
Ala	Glu	Arg	Arg	Gly	Asp	Leu	Asp	Lys	Ala	Tyr	Thr	Lys	Leu	Ile
				290					295					300
Arg	Gly	Val	Phe	Val	Asn	Val	Glu	Lys	Val	Ala	Asn	Glu	Ser	Gln
				305					310					315
Lys	Thr	Pro	Arg	Asp	Val	Val	Met	Met	Glu	Asn	Phe	His	His	Ile
				320					325					330
Phe	Ala	Thr	Leu	Ser	Arg	Leu	Lys	Ile	Ser	Cys	Leu	Glu	Ala	Glu
				335					340					345
Lys	Lys	Glu	Ala	Ala	Ile	Asn	His	Lys	Phe	Phe				
				350					355					

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<210> 59
<211> 299
<212> PRT
<213> Homo sapiens
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<220>  
<221> misc_feature  
<223> Incyte clone 2280456CD1
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<400> 59														
Met	Glu	Glu	Leu	Leu	Pro	Asp	Gly	Gln	Ile	Trp	Ala	Asn	Met	Asp
1				5					10					15
Pro	Glu	Glu	Arg	Met	Leu	Ala	Ala	Ala	Thr	Ala	Phe	Thr	His	Ile
				20					25					30
Cys	Ala	Gly	Gln	Gly	Glu	Gly	Asp	Val	Arg	Arg	Glu	Ala	Gln	Ser
				35					40					45
Ile	Gln	Tyr	Asp	Pro	Tyr	Ser	Lys	Ala	Ser	Val	Ala	Pro	Gly	Lys
				50					55					60
Arg	Pro	Ala	Leu	Pro	Val	Gln	Leu	Gln	Tyr	Pro	His	Val	Glu	Ser
				65					70					75
Asn	Val	Pro	Ser	Glu	Thr	Val	Ser	Glu	Ala	Ser	Gln	Arg	Leu	Arg
				80					85					90
Lys	Pro	Val	Met	Lys	Arg	Lys	Val	Leu	Arg	Arg	Lys	Pro	Asp	Gly
				95					100					105
Glu	Val	Leu	Val	Thr	Asp	Glu	Ser	Ile	Ile	Ser	Glu	Ser	Glu	Ser
				110					115					120
Gly	Thr	Glu	Asn	Asp	Gln	Asp	Leu	Trp	Asp	Leu	Arg	Gln	Arg	Leu
				125					130					135

Met	Asn	Val	Gln	Phe	Gln	Glu	Asp	Lys	Glu	Ser	Ser	Phe	Asp	Val
				140					145					150
Ser	Gln	Lys	Phe	Asn	Leu	Pro	His	Glu	Tyr	Gln	Gly	Ile	Ser	Gln
				155					160					165
Asp	Gln	Leu	Ile	Cys	Ser	Leu	Gln	Arg	Glu	Gly	Met	Gly	Ser	Pro
				170					175					180
Ala	Tyr	Glu	Gln	Asp	Leu	Ile	Val	Ala	Ser	Arg	Pro	Lys	Ser	Phe
				185					190					195
Ile	Leu	Pro	Lys	Leu	Asp	Gln	Leu	Ser	Arg	Asn	Arg	Gly	Lys	Thr
				200					205					210
Asp	Arg	Val	Ala	Arg	Tyr	Phe	Glu	Tyr	Lys	Arg	Asp	Trp	Asp	Ser
				215					220					225
Ile	Arg	Leu	Pro	Gly	Glu	Asp	His	Arg	Lys	Glu	Leu	Arg	Trp	Gly
				230					235					240
Val	Arg	Glu	Gln	Met	Leu	Cys	Arg	Ala	Glu	Pro	Gln	Ser	Lys	Pro
				245					250					255
Gln	His	Ile	Tyr	Val	Pro	Asn	Asn	Tyr	Leu	Val	Pro	Thr	Glu	Lys
				260					265					270
Lys	Arg	Ser	Ala	Leu	Arg	Trp	Gly	Val	Arg	Cys	Asp	Leu	Ala	Asn
				275					280					285
Gly	Val	Ile	Pro	Arg	Lys	Leu	Pro	Phe	Pro	Leu	Ser	Pro	Ser	
				290					295					

&lt;210&gt; 60

&lt;211&gt; 293

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2284580CD1

&lt;400&gt; 60

Met	Ala	Thr	Phe	Ser	Gly	Pro	Ala	Gly	Pro	Ile	Leu	Ser	Leu	Asn
1				5					10					15
Pro	Gln	Glu	Asp	Val	Glu	Phe	Gln	Lys	Glu	Val	Ala	Gln	Val	Arg
				20					25					30
Lys	Arg	Ile	Thr	Gln	Arg	Lys	Lys	Gln	Glu	Gln	Leu	Thr	Pro	Gly
				35					40					45
Val	Val	Tyr	Val	Arg	His	Leu	Pro	Asn	Leu	Leu	Asp	Glu	Thr	Gln
				50					55					60
Ile	Phe	Ser	Tyr	Phe	Ser	Gln	Phe	Gly	Thr	Val	Thr	Arg	Phe	Arg
				65					70					75
Leu	Ser	Arg	Ser	Lys	Arg	Thr	Gly	Asn	Ser	Lys	Gly	Tyr	Ala	Phe
				80					85					90
Val	Glu	Phe	Glu	Ser	Glu	Asp	Val	Ala	Lys	Ile	Val	Ala	Glu	Thr
				95					100					105
Met	Asn	Asn	Tyr	Leu	Phe	Gly	Glu	Arg	Leu	Leu	Glu	Cys	His	Phe
				110					115					120
Met	Pro	Pro	Glu	Lys	Val	His	Lys	Glu	Leu	Phe	Lys	Asp	Trp	Asn
				125					130					135
Ile	Pro	Phe	Lys	Gln	Pro	Ser	Tyr	Pro	Ser	Val	Lys	Arg	Tyr	Asn
				140					145					150
Arg	Asn	Arg	Thr	Leu	Thr	Gln	Lys	Leu	Arg	Met	Glu	Glu	Arg	Phe
				155					160					165
Lys	Lys	Lys	Glu	Arg	Leu	Leu	Arg	Lys	Lys	Leu	Ala	Lys	Lys	Gly
				170					175					180
Ile	Asp	Tyr	Asp	Phe	Pro	Ser	Leu	Ile	Leu	Gln	Lys	Thr	Glu	Ser
				185					190					195
Ile	Ser	Lys	Thr	Asn	Arg	Gln	Thr	Ser	Thr	Lys	Gly	Gln	Val	Leu
				200					205					210

Arg	Lys	Lys	Lys	Lys	Lys	Val	Ser	Gly	Thr	Leu	Asp	Thr	Pro	Glu
				215					220					225
Lys	Thr	Val	Asp	Ser	Gln	Gly	Pro	Thr	Pro	Val	Cys	Thr	Pro	Thr
				230					235					240
Phe	Leu	Glu	Arg	Arg	Lys	Ser	Gln	Val	Ala	Glu	Leu	Asn	Asp	Asp
				245					250					255
Asp	Lys	Asp	Asp	Glu	Ile	Val	Phe	Lys	Gln	Pro	Ile	Ser	Cys	Val
				260					265					270
Lys	Glu	Glu	Ile	Gln	Glu	Thr	Gln	Thr	Pro	Thr	His	Ser	Arg	Lys
				275					280					285
Lys	Arg	Arg	Arg	Ser	Ser	Asn	Gln							
				290										

&lt;210&gt; 61

&lt;211&gt; 777

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;223&gt; Incyte clone 2779172CD1

&lt;400&gt; 61

Met	Val	Leu	Cys	His	Ser	Phe	Leu	Tyr	Arg	Ile	Leu	Thr	Val	Gln
1				5					10					15
Gln	His	Gly	Phe	Phe	Phe	Gly	His	Asp	Arg	Arg	Pro	Ala	Asp	Gly
				20					25					30
Glu	Lys	Gln	Ala	Ala	Thr	His	Val	Ser	Leu	Asp	Gln	Glu	Tyr	Asp
				35					40					45
Ser	Glu	Ser	Ser	Gln	Gln	Trp	Arg	Glu	Leu	Glu	Glu	Gln	Val	Val
				50					55					60
Ser	Val	Val	Asn	Lys	Gly	Val	Ile	Pro	Ser	Asn	Phe	His	Pro	Thr
				65					70					75
Gln	Tyr	Cys	Leu	Asn	Ser	Tyr	Ser	Asp	Asn	Ser	Arg	Phe	Pro	Leu
				80					85					90
Ala	Val	Val	Glu	Glu	Pro	Ile	Thr	Val	Glu	Val	Ala	Phe	Arg	Asn
				95					100					105
Pro	Leu	Lys	Val	Leu	Leu	Leu	Leu	Thr	Asp	Leu	Ser	Leu	Leu	Trp
				110					115					120
Lys	Phe	His	Pro	Lys	Asp	Phe	Ser	Gly	Lys	Asp	Asn	Glu	Glu	Val
				125					130					135
Lys	Gln	Leu	Val	Thr	Ser	Glu	Pro	Glu	Met	Ile	Gly	Ala	Glu	Val
				140					145					150
Ile	Ser	Glu	Phe	Leu	Ile	Asn	Gly	Glu	Glu	Ser	Lys	Val	Ala	Arg
				155					160					165
Leu	Lys	Leu	Phe	Pro	His	His	Ile	Gly	Glu	Leu	His	Ile	Leu	Gly
				170					175					180
Val	Val	Tyr	Asn	Leu	Gly	Thr	Ile	Gln	Gly	Ser	Met	Thr	Val	Asp
				185					190					195
Gly	Ile	Gly	Ala	Leu	Pro	Gly	Cys	His	Thr	Gly	Lys	Tyr	Ser	Leu
				200					205					210
Ser	Met	Ser	Val	Arg	Gly	Lys	Gln	Asp	Leu	Glu	Ile	Gln	Gly	Pro
				215					220					225
Arg	Leu	Asn	Asn	Thr	Lys	Glu	Glu	Lys	Thr	Ser	Val	Lys	Tyr	Gly
				230					235					240
Pro	Asp	Arg	Arg	Leu	Asp	Pro	Ile	Ile	Thr	Glu	Glu	Met	Pro	Leu
				245					250					255
Leu	Glu	Val	Phe	Phe	Ile	His	Phe	Pro	Thr	Gly	Leu	Leu	Cys	Gly
				260					265					270
Glu	Ile	Arg	Lys	Ala	Tyr	Val	Glu	Phe	Val	Asn	Val	Ser	Lys	Cys
				275					280					285

Pro	Leu	Thr	Gly	Leu	Lys	Val	Val	Ser	Lys	Arg	Pro	Glu	Phe	Phe
				290					295					300
Thr	Phe	Gly	Gly	Asn	Thr	Ala	Val	Leu	Thr	Pro	Leu	Ser	Pro	Ser
				305					310					315
Ala	Ser	Glu	Asn	Cys	Ser	Ala	Tyr	Lys	Thr	Val	Val	Thr	Asp	Ala
				320					325					330
Thr	Ser	Val	Cys	Thr	Ala	Leu	Ile	Ser	Ser	Ala	Ser	Ser	Val	Asp
				335					340					345
Phe	Gly	Ile	Gly	Thr	Gly	Ser	Gln	Pro	Glu	Val	Ile	Pro	Val	Pro
				350					355					360
Leu	Pro	Asp	Thr	Val	Leu	Leu	Pro	Gly	Ala	Ser	Val	Gln	Leu	Pro
				365					370					375
Met	Trp	Leu	Arg	Gly	Pro	Asp	Glu	Glu	Gly	Val	His	Glu	Ile	Asn
				380					385					390
Phe	Leu	Phe	Tyr	Tyr	Glu	Ser	Val	Lys	Lys	Gln	Pro	Lys	Ile	Arg
				395					400					405
His	Arg	Ile	Leu	Arg	His	Thr	Ala	Ile	Ile	Cys	Thr	Ser	Arg	Ser
				410					415					420
Leu	Asn	Val	Arg	Ala	Thr	Val	Cys	Arg	Ser	Asn	Ser	Leu	Glu	Asn
				425					430					435
Glu	Glu	Gly	Arg	Gly	Gly	Asn	Met	Leu	Val	Phe	Val	Asp	Val	Glu
				440					445					450
Asn	Thr	Asn	Thr	Ser	Glu	Ala	Gly	Val	Lys	Glu	Phe	His	Ile	Val
				455					460					465
Gln	Val	Ser	Ser	Ser	Ser	Lys	His	Trp	Lys	Leu	Gln	Lys	Ser	Val
				470					475					480
Asn	Leu	Ser	Glu	Asn	Lys	Asp	Thr	Lys	Leu	Ala	Ser	Arg	Glu	Lys
				485					490					495
Gly	Lys	Phe	Cys	Phe	Lys	Ala	Ile	Arg	Cys	Glu	Lys	Glu	Glu	Ala
				500					505					510
Ala	Thr	Gln	Ser	Ser	Glu	Lys	Tyr	Thr	Phe	Ala	Asp	Ile	Ile	Phe
				515					520					525
Gly	Asn	Glu	Gln	Ile	Ile	Ser	Ser	Ala	Ser	Pro	Cys	Ala	Asp	Phe
				530					535					540
Phe	Tyr	Arg	Ser	Leu	Ser	Ser	Glu	Leu	Lys	Lys	Pro	Gln	Ala	His
				545					550					555
Leu	Pro	Val	His	Thr	Glu	Lys	Gln	Ser	Thr	Glu	Asp	Ala	Val	Arg
				560					565					570
Leu	Ile	Gln	Lys	Cys	Ser	Glu	Val	Asp	Leu	Asn	Ile	Val	Ile	Leu
				575					580					585
Trp	Lys	Ala	Tyr	Val	Val	Glu	Asp	Ser	Lys	Gln	Leu	Ile	Leu	Glu
				590					595					600
Gly	Gln	His	His	Val	Ile	Leu	Arg	Thr	Ile	Gly	Lys	Glu	Ala	Phe
				605					610					615
Ser	Tyr	Pro	Gln	Lys	Gln	Glu	Pro	Pro	Glu	Met	Glu	Leu	Leu	Lys
				620					625					630
Phe	Phe	Arg	Pro	Glu	Asn	Ile	Thr	Val	Ser	Ser	Arg	Pro	Ser	Val
				635					640					645
Glu	Gln	Leu	Ser	Ser	Leu	Ile	Lys	Thr	Ser	Leu	His	Tyr	Pro	Glu
				650					655					660
Ser	Phe	Asn	His	Pro	Phe	His	Gln	Lys	Ser	Leu	Cys	Leu	Val	Pro
				665					670					675
Val	Thr	Leu	Leu	Leu	Ser	Asn	Cys	Ser	Lys	Ala	Asp	Val	Asp	Val
				680					685					690
Ile	Val	Asp	Leu	Arg	His	Lys	Thr	Thr	Ser	Pro	Glu	Ala	Leu	Glu
				695					700					705
Ile	His	Gly	Ser	Phe	Thr	Trp	Leu	Gly	Gln	Thr	Gln	Tyr	Lys	Leu
				710					715					720
Gln	Leu	Lys	Ser	Gln	Glu	Ile	His	Ser	Leu	Gln	Leu	Lys	Ala	Cys
				725					730					735
Phe	Val	His	Thr	Gly	Val	Tyr	Asn	Leu	Gly	Thr	Pro	Arg	Val	Phe
				740					745					750
Ala	Lys	Leu	Ser	Asp	Gln	Val	Thr	Val	Phe	Glu	Thr	Ser	Gln	Gln
				755					760					765

Asn Ser Met Pro Ala Leu Ile Ile Ile Ser Asn Val  
 770 775

<210> 62  
 <211> 97  
 <212> PRT  
 <213> Homo sapiens  
 <220>  
 <221> misc\_feature  
 <223> Incyte clone 3279329CD1

<400> 62  
 Met Pro Pro Gly Thr Val Leu Arg Tyr Val Gln Cys Leu Phe Leu  
 1 5 10 15  
 Asp Leu Cys Ile Cys His Glu Ala Pro Cys Gly Leu Cys Met Lys  
 20 25 30  
 Leu Leu Leu Cys Phe Trp Val Asn Arg Cys Ala Cys Gln Leu Ala  
 35 40 45  
 Cys Val Leu Ser Lys Phe His Lys Leu Lys Val Phe Lys Gly Cys  
 50 55 60  
 Val Val Ser Glu Leu Tyr Val Ser Phe Leu Ser Leu Tyr Leu Gln  
 65 70 75  
 Arg Val Arg Asn Glu Ile Tyr Thr Ser Lys Val Ser Leu Ile Asn  
 80 85 90  
 Met Ala Phe Cys Phe Ser Met  
 95

<210> 63  
 <211> 308  
 <212> PRT  
 <213> Homo sapiens  
 <220>  
 <221> misc\_feature  
 <223> Incyte clone 3340290CD1

<400> 63  
 Met Ser Val Ser Gly Leu Lys Ala Glu Leu Lys Phe Leu Ala Ser  
 1 5 10 15  
 Ile Phe Asp Lys Asn His Glu Arg Phe Arg Ile Val Ser Trp Lys  
 20 25 30  
 Leu Asp Glu Leu His Cys Gln Phe Leu Val Pro Gln Gln Gly Ser  
 35 40 45  
 Pro His Ser Leu Pro Pro Pro Leu Thr Leu His Cys Asn Ile Thr  
 50 55 60  
 Glu Ser Tyr Pro Ser Ser Ser Pro Ile Trp Phe Val Asp Ser Glu  
 65 70 75  
 Asp Pro Asn Leu Thr Ser Val Leu Glu Arg Leu Glu Asp Thr Lys  
 80 85 90  
 Asn Asn Asn Leu Asn Gly Thr Thr Glu Glu Val Thr Ser Glu Glu  
 95 100 105  
 Glu Glu Glu Glu Glu Glu Met Ala Glu Asp Ile Glu Asp Leu Asp  
 110 115 120  
 His Tyr Glu Met Lys Glu Glu Glu Pro Ile Ser Gly Lys Lys Ser  
 125 130 135  
 Glu Asp Glu Gly Ile Glu Lys Glu Asn Leu Ala Ile Leu Glu Lys  
 140 145 150  
 Ile Arg Lys Thr Gln Arg Gln Asp His Leu Asn Gly Ala Val Ser  
 155 160 165

[illegible]

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<210> 64
<211> 290
<212> PRT
<213> Homo sapiens
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<220>  
<221> misc_feature  
<223> Incyte clone 3376404CD1
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<400> 64														
Met	Arg	Arg	Pro	Ala	Ala	Val	Pro	Leu	Leu	Leu	Leu	Leu	Cys	Phe
1				5					10					15
Gly	Ser	Gln	Arg	Ala	Lys	Ala	Ala	Thr	Ala	Cys	Gly	Arg	Pro	Arg
				20					25					30
Met	Leu	Asn	Arg	Met	Val	Gly	Gly	Gln	Asp	Thr	Gln	Glu	Gly	Glu
				35					40					45
Trp	Pro	Trp	Gln	Val	Ser	Ile	Gln	Arg	Asn	Gly	Ser	His	Phe	Cys
				50					55					60
Gly	Gly	Ser	Leu	Ile	Ala	Glu	Gln	Trp	Val	Leu	Thr	Ala	Ala	His
				65					70					75
Cys	Phe	Arg	Asn	Thr	Ser	Glu	Thr	Ser	Leu	Tyr	Gln	Val	Leu	Leu
				80					85					90
Gly	Ala	Arg	Gln	Leu	Val	Gln	Pro	Gly	Pro	His	Ala	Met	Tyr	Ala
				95					100					105
Arg	Val	Arg	Gln	Val	Glu	Ser	Asn	Pro	Leu	Tyr	Gln	Gly	Thr	Ala
				110					115					120
Ser	Ser	Ala	Asp	Val	Ala	Leu	Val	Glu	Leu	Glu	Ala	Pro	Val	Pro
				125					130					135
Phe	Thr	Asn	Tyr	Ile	Leu	Pro	Val	Cys	Leu	Pro	Asp	Pro	Ser	Val
				140					145					150
Ile	Phe	Glu	Thr	Gly	Met	Asn	Cys	Trp	Val	Thr	Gly	Trp	Gly	Ser
				155					160					165
Pro	Ser	Glu	Glu	Asp	Leu	Leu	Pro	Glu	Pro	Arg	Ile	Leu	Gln	Lys
				170					175					180
Leu	Ala	Val	Pro	Ile	Ile	Asp	Thr	Pro	Lys	Cys	Asn	Leu	Leu	Tyr
				185					190					195
Ser	Lys	Asp	Thr	Glu	Phe	Gly	Tyr	Gln	Pro	Lys	Thr	Ile	Lys	Asn
				200					205					210
Asp	Met	Leu	Cys	Ala	Gly	Phe	Glu	Glu	Gly	Lys	Lys	Asp	Ala	Cys
				215					220					225
Lys	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Leu	Val	Gly	Gln	Ser
				230					235					240

Trp	Leu	Gln	Ala	Gly	Val	Ile	Ser	Trp	Gly	Glu	Gly	Cys	Ala	Arg
				245					250					255
Gln	Asn	Arg	Pro	Gly	Val	Tyr	Ile	Arg	Val	Thr	Ala	His	His	Asn
				260					265					270
Trp	Ile	His	Arg	Ile	Ile	Pro	Lys	Leu	Gln	Phe	Gln	Pro	Ala	Arg
				275					280					285
Leu	Gly	Gly	Gln	Lys										
				290										

<210> 65  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 4173111CD1

Met	Glu	Met	Ser	Gly	Leu	Ser	Phe	Ser	Glu	Met	Glu	Gly	Cys	Arg
1				5					10					15
Asn	Leu	Leu	Gly	Leu	Leu	Asp	Asn	Asp	Glu	Ile	Met	Ala	Leu	Cys
				20					25					30
Asp	Thr	Val	Thr	Asn	Arg	Leu	Val	Gln	Pro	Gln	Asp	Arg	Gln	Asp
				35					40					45
Ala	Val	His	Ala	Ile	Leu	Ala	Tyr	Ser	Gln	Ser	Ala	Glu	Glu	Leu
				50					55					60
Leu	Arg	Arg	Arg	Lys	Val	His	Arg	Glu	Val	Ile	Phe	Lys	Tyr	Leu
				65					70					75
Ala	Thr	Gln	Gly	Ile	Val	Ile	Pro	Pro	Ala	Thr	Glu	Lys	His	Asn
				80					85					90
Leu	Ile	Gln	His	Ala	Lys	Asp	Tyr	Trp	Gln	Lys	Gln	Pro	Gln	Leu
				95					100					105
Lys	Leu	Lys	Glu	Thr	Pro	Glu	Pro	Val	Thr	Lys	Thr	Glu	Asp	Ile
				110					115					120
His	Leu	Phe	Gln	Gln	Gln	Val	Lys	Glu	Asp	Lys	Lys	Ala	Glu	Lys
				125					130					135
Val	Asp	Phe	Arg	Arg	Leu	Gly	Glu	Glu	Phe	Cys	His	Trp	Phe	Phe
				140					145					150
Gly	Leu	Leu	Asn	Ser	Gln	Asn	Pro	Phe	Leu	Gly	Pro	Pro	Gln	Asp
				155					160					165
Glu	Trp	Gly	Pro	Gln	His	Phe	Trp	His	Asp	Val	Lys	Leu	Arg	Phe
				170					175					180
Tyr	Tyr	Asn	Thr	Ser	Glu	Gln	Asn	Val	Met	Gly	Leu	Thr	Met	Glu
				185					190					195
Pro	Glu	Ser												

<210> 66  
 <211> 789  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 001106CB1

<400> 66  
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 cgaaacagga agtcccgccc ctctatggaa agtaaattgg agctcggaag ggtcaaaaaga 120  
 gtccgcggtt tcgccgcgtg agttgctttt tgcggctggg gaggtctacg cttctagagc 180



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ttgagccagc ggggcgaccc tgcagtggca ggactcggca ccgcgcctc caccgccggt 240
tggtagcctg cgtgacagtt tcctcccgtc .gacatcgaaa ggaagccgga cgtgggcggg 300
cagagagctt catcgagta ggaatggcag ccccatctat gaaggaaaga caggtctgct 360
ggggggcccg ggatgagtac tggaaagtgt tagatgagaa cttagaggat gcttctcaat 420
gcaagaagtt aagaagctct ttcgaatcaa gttgtcccca acagtggata aaatatattg 480
ataaaaagaag agactactta aaattcaaaag aaaaatttga agcaggacaa tttgagcctt 540
cagaaacaac tgcaaaatcc taggctgttc ataaagattg aaagtattct ttctggacat 600
tgaaaaagct ccactgacta tggaaacagta atagtttgaa tcatagttaa catcaatact 660
tgttccctat atacgacact tgataattaa gatgatcaag aaccagaaga tctgtgaaga 720
aatgaaataa aatgggtattt agtaagaaat ctctatttta agaaaaaaag taaaacctgt 780
tataaaca 789

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&lt;210&gt; 67

&lt;211&gt; 1117

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 004586CB1

&lt;400&gt; 67

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&lt;210&gt; 68

&lt;211&gt; 1628

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 052927CB1

&lt;400&gt; 68

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&lt;211&gt; 1706

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 082843CB1

&lt;400&gt; 69

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&lt;211&gt; 1864

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&lt;211&gt; 3685

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte clone 673766CB1

&lt;400&gt; 72

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 <213> Homo sapiens

<220>  
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 <223> Incyte clone 1504753CB1

<400> 73  
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&lt;210&gt; 74

&lt;211&gt; 1578

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1760185CB1

&lt;400&gt; 74

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 <211> 1624  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1805061CB1

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 <212> DNA  
 <213> Homo sapiens

<220>  
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 <223> Incyte clone 1850120CB1

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<211> 1319

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte clone 1852290CB1

<400> 77

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<212> DNA

<213> Homo sapiens

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<223> Incyte clone 1944530CB1

<400> 78

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&lt;210&gt; 79

&lt;211&gt; 1963

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2019742CB1

&lt;400&gt; 79

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 <211> 1089  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc feature  
 <223> Incyte clone 2056042CB1

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 <213> Homo sapiens

<220>  
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&lt;211&gt; 3963

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&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2724537CB1

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&lt;223&gt; Incyte clone 025818CB1

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tgcaaaacat agaattgtcta caggagagaa acctcacaag tgtgatgatt gtgggcaagc 2040
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&lt;210&gt; 87

&lt;211&gt; 2358

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 619699CB1

&lt;400&gt; 87

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2358

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&lt;210&gt; 88

&lt;211&gt; 1978

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 693452CB1

&lt;400&gt; 88

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&lt;210&gt; 89

&lt;211&gt; 2084

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;223&gt; Incyte clone 839651CB1

&lt;400&gt; 89

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&lt;210&gt; 90

&lt;211&gt; 2024

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1253545CB1

&lt;400&gt; 90

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&lt;210&gt; 91

&lt;211&gt; 3518

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1425691CB1

&lt;400&gt; 91

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&lt;210&gt; 92

&lt;211&gt; 2741

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1484257CB1

&lt;400&gt; 92

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&lt;211&gt; 3247

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte clone 2076520CB1

&lt;400&gt; 97

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&lt;211&gt; 2348

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2291241CB1

&lt;400&gt; 98

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 <223> Incyte clone 2474110CB1

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&lt;211&gt; 608

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&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2661254CB1

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte clone 2674047CB1

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&lt;211&gt; 1945

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;223&gt; Incyte clone 2762174CB1

&lt;400&gt; 104

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&lt;211&gt; 1829

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&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte clone 2765991CB1

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<220>  
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 <212> DNA  
 <213> Homo sapiens

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 <213> Homo sapiens

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&lt;211&gt; 2133

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte clone 156986CB1

&lt;400&gt; 111

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 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 319415CB1

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<400> 112
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atgtgtcttc agaggagccc aaagagctca tgggtccatgt ggggtggattg attcagatgg 540
gatgtgtttt ccagagcaca gaagtgaaac acgtgaccaa ggtagaatgg atattttcag 600
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aatcattcct ctggcaaaaa aaaaaaaaaa 1649
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<210> 113  
 <211> 714  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 635581CB1

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<400> 113
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aaagattatg agatcctgaa aaaggaaacg aacaagttca tcttgagaat ttatacacac 420
tggtcgagaa gaagcatcct caggaaaggt tcaaaaggca tgcagaatct ctagttaggc 480
cgatcagtga ggatctttct ctgtacagag ccagaccaca aagactggga ngggtgatat 540
tttttcaa atgcttgatcc caacatgatg ttaaaagaca caccaagaaa taaggaaaca 600
tggcacaatc aaagagtcaa aattatccag gaccctactt taaggaaacc cagttatctt 660
ccattatcct cagaaggatt tccagcctaa ccaccattaa acatgttcac gtgg 714
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<210> 114  
 <211> 1165  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 921803CB1

<400> 114  
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 ttcggcggcg ggaacagggt ccggcgccctc cgccccatcc ccaggggccg cctcccccg 180  
 ggcgggcctcc aggcgtgccga gacctataaa ggcgccagggt tttctcaatg aagccgggac 240  
 gcaactccga gcgcaactgc tggctgcacc ctaccggggc tgccttgga gtcgtccccg 300  
 ccgccccctc gcaccggcat gaagctcctc gtgggcatcg gaggcatgac caacggcggc 360  
 aagaccacgc tgaccaacag cctgctcaga gccctgccc actgctgcgt gatccatcag 420  
 gatgacttct tcaagcccca agaccaaata gcagttgggg aagacggctt caaacagtgg 480  
 gacgtgctgg agtctctgga catggaggcc atgctggaca ccgtgcaggc ctggctgagc 540  
 agcccgacga agtttgcccg tgcccacggg gtcagcgtcc agccagaggc ctcgacacc 600  
 cacatcctcc tcctggaagg cttcctgctc tacagctaca agcccctggt ggacttgtag 660  
 agccgcccgt acttctgac cgtcccgtat gaagagtgc aagtggaggag aagtacccgc 720  
 aactacacag tccctgatcc ccccgccctc ttcgatggcc acgtgtggcc catgtaccag 780  
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 tgcgccacac gaacggccag gcctgcagcg tcccagcagg acagcatgtg agcgtttccc 1020  
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<210> 115  
 <211> 2143  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 1250492CB1

<400> 115  
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 gggacggatg tctaatacctg cacctagctg ggttggtcag tagaacctat tttcagactc 480  
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<210> 116

<211> 1010

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte clone 1427838CB1

<400> 116

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catggagaat gatgaacttc cgtcagcgga tgggatggat tggagtggga ttgtatctgt 240
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<210> 117

<211> 2059

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte clone 1448258CB1

<400> 117

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acaagagaag ctgcagcaat gggacctact aagtttacac aaactaatar agggataata 180
gaaaataaac tcttggaagc ccctgatgtt ttatgcctca ggcttagtac tgaacaatgc 240
caagcacatg aggagaaagg catagaggaa ctgagtgtat cctctgggcc caaatcctat 300
agtataacag agaaacacta tgcacaggag gatcccagga tgttattttg agcagctgtt 360
gatcatagta gttcaggaga tatgtctttg ttaccagct cagatcctaa gtttcaagga 420
cttggagtgg ttgagtcagc agtaactgca aacaacacag aagaaagctt attccgtatt 480
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gaagtattgc tgtttacaga tcagactgat gatttggcta aagaggaacc aacttcttta 600
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&lt;210&gt; 118

&lt;211&gt; 2273

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc feature

&lt;223&gt; Incyte clone 1645941CB1

&lt;400&gt; 118

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&lt;210&gt; 119

&lt;211&gt; 1772

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1646005CB1

&lt;400&gt; 119

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&lt;210&gt; 120

&lt;211&gt; 2260

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1686561CB1

&lt;400&gt; 120

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atcagaacca tacccaagtc agttgctgaa accaatccca gaatattccc cggaagagga 180
atcagaacca cctgctccaa atataaggaa catggcacc cagagcttgt ctgcacccac 240
aatgcttcac aattcctccg gagacttttc tcaagctcac tcaaccctga aacttgcaaa 300
tcaccagcgg cctgtatccc ggcaggtcac ctgcctgcgc actcaagttc tggaggacag 360
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cactggccat gactcagaca aatcagacca aagtttacct aatgcctcag cagactcctt 600
gggcggtagc caggagatgg tgcaacggcc ccagcctcac aggaaccgag caggcctgga 660
tctgccaaac atagacacgg gatatgattc ccagccccag gatgtcctgg gcatcaggca 720
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gcctcccaat ctttcccccac atgtctccatg gaactatcat taccattgtc ctggaagtcc 900
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aatgatgcag attgagttca taaaacaagg aagcatgaat ttcagattca tccctgtgct 1620
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ataatgtaag ggatgtggca gcaaattgaa atgactacaa acactctcct atcaatcact 2160
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tacaataaat aaaatgttta ctcttttgta aaaaaaaaaa 2260

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&lt;210&gt; 121

&lt;211&gt; 1602

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1821233CB1

&lt;400&gt; 121

```

gccaagacc gtgcgcgaca cgctgctggc gctgcaccag cacggccact cggggccctt 60
cgagagcaag ttaagaagg agccggcctt gactgcaggc aggttggttg gtttcgaggc 120
caacggggcc aacgggtcta aagcagttgc aagaacagca aggaaaagga agccctctcc 180
agaaccagaa ggtgaagtgc ggccccctaa gatcaacgga gaggccagc cgtggctgtc 240
cacatccaca gaggggctca agatccccat gactcctaca tctctttttg tgtctccgcc 300
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ccagtcccc atggcagccc tgatcttagt agcagacaat gcagggggca gtcatgcctc 420
aaaagatgcc aaccaggttc actccactac caggaggaat agcaacagtc gcacctctcc 480
gtcctctatg aaccaaagaa ggctgggtcc cagagaggtg gggggccagg gagcaggcaa 540
cacaggagga ctggagccag tgcaccctgc cagcctcccc gactcctctc tggcaaccag 600
tgccccgctg tgctgcaccc tctgccacga gcggctggag gacacccatt ttgtgcagt 660
cccgtccgtc ccttcgcaca agttctgctt cccttgctcc agacaaagca tcaaacagca 720
gggagctagt ggagaggtct attgtcccag tggggaaaaa tgccctcttg tgggtccaa 780

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tgtcccctgg gcctttatgc aaggggaaat tgcaaccatc cttgctggag atgtgaaagt 840
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ttaaaactgc ttgaattgta tatatatctc catatatata tatatccaag acaagggaaa 960
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cagtttacct tgaaacattg tcctcagagg agtaggaaa tggttttga atctctattt 1440
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gattgtgtgg tcttttgggg ttttttgttt tttttttttt aagacaaaag tgaccgctgt 1560
tcactgtcca cgtgatcagt tgtaagatta caatgctgca tc 1602

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&lt;210&gt; 122

&lt;211&gt; 1655

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1877278CB1

&lt;400&gt; 122

```

gcgggcgcac tccggtgcaa gcgaggacac gacacatgca gtggcttctg gactgcgcca 60
tgactggacg caagtaactt ctaggctctg agacaagagg aagagaagat gaaggaagac 120
tgtctgccga gttctcacgt gcccatcagt gacagcaagt ccattcagaa gtcggagctc 180
ttaggcctgc tgaaaacctt caactgctac catgagggca agagcttcca gctgagacac 240
cgtgaggaag aagggaactt gatcatcgag gggctcctca acattgcctg ggggctgag 300
cggcccatcc ggctgcagat gcaggatgac cgggagcagg tgcacctccc ctccacctca 360
tggtgcccc gacggcctag ctgccctcta aaggagccat cgccccagaa cgggaacatc 420
acagcccagg ggccaagcat tcagccagtg cacaaggctg agagttccac agacagctcg 480
gggcccctgg aggaggcaga ggaggcccc cagctgatgc ggaccaagag cgacgccagt 540
tgcatgagcc agaggaggcc caagtgccgc gccccgggtg aggccagcg catccggcga 600
caccggttct ctatcaacgg ccacttctac aatcataaga cctccgtgtt tactccagcc 660
tatggatccg tgaccaatgt gagggccaac agcaccatga caaccctgca ggtgctcacc 720
ctgctgctga acaaatttag ggtggaagat ggccccagtg agttcgact ctacatcggt 780
cacgagtctg gggagcggac aaaattaaaa gactgcgagt acccgctgat ttccagaatc 840
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gctcagcccc aacacagagg tgagaccagg aataa 1655

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&lt;210&gt; 123

&lt;211&gt; 2225

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 1880692CB1

&lt;400&gt; 123

```

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atgccaagct gatggagtgg ctaaagagta cagattatgg aaaatatgaa ggactaacia 180
agaattacat ggattattta tcccgactat atgaaagaga aatcaaagat ttctttgaag 240
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gttcggggaa attaaactga tctacttcta gtctaaataa gctcagtgtt cagagttcag 360
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aacataattg tggcacacca ctgcctgttt catctgagaa agatatgac cgccaaatga 660
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aaattgatag ctttaactct ctttatatgt tagtcaaaat gagtcatcat gtgtggactg 780
cacaaaatgt ggaccctgct tctttcctaa gtactacatt gggaaatgtt ttggtgactg 840
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gagataccga tatgcttctc ttttttggct tttcttattg cttccattaa ggattttcat 1560
tccagtttga tacatcattt ctgcttctct catctgccgt ctcttagcag cctcttcttc 1620
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cttc 2225

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&lt;210&gt; 124

&lt;211&gt; 1516

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2280456CB1

&lt;400&gt; 124

```

cggatttaaa ctcagcggg cggcggttaa ccgcaggctc ggcgcgtggg ccggcagtg 60
gcctgcgcaa gttacgcgaa agctaacaga atctgcggtg ctctgctggc gactggcatg 120
acgcggtgca gagagcggac ttccgcgacg cgggtgtttt tttttacttg aatgtaaata 180
ccaatcaaga tacattgaaa taagaaggtc ctacagtgtg ggggaagcaa tggagaact 240
tctacctgat ggacaaatg gggctaata ggatccagaa gaacgaatgt tggcagctgc 300
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tcctgtgcaa ctacagtacc cacatgtaga aagtaatgtc ccttcagaaa cagtctctg 480
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tggggaagta ttagtaacag atgagtcgat tatcagtga tcagaatctg gtacagaaaa 600
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```



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ctcaatacgt ttacctggtg aagatcatag aaaggaatta cgctggggtg tccgagagca 960
gatgctttgt cgagcagaac cccaatccaa acctcagcat atatatgtcc caaacaatta 1020
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tgcttcagtg tgtgtttttt aagttgctgg gcattacact taccaattaa agaatttttg 1500
aaattcaaaa aaaaaa 1516

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&lt;210&gt; 125

&lt;211&gt; 1635

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2284580CB1

&lt;400&gt; 125

```

cgggggagct gggagcccga cgtttccggg agcgccgcgt ggttagcgct ggcggtttt 60
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gtcaggtttc aaaaggaggt ggcgcaggtt cgcaagcgca taaccagcg aaaaaaaca 180
gaacaactta ctcttgaggt agtctatgtg cgccacctac ctaacctact tgacgaaacc 240
cagatctttt catatttctc ccagtttggc actgtgacac ggttcagcgt gtccagaagt 300
aaaaggactg gaaatagcaa aggctatgca tttgtggagt ttgagtctga ggatgttgcc 360
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cagccatcat atccatcagt gaaacgggat aatcggaatc ggacactaac acaaaagcta 540
cggatggagg agcgatttaa aaagaaagaa agattactca ggaagaaatt agctaaaaaa 600
ggaattgact atgattttcc ttctttgatt ttacagaaaa cggaaagtat ttcaaaaaat 660
aatcgctcaga cgtctacaaa aggccagggt ttacgtaaga agaagaaaaa agtttcaggt 720
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atctcttttg aaaaatataa tatttttatg agagtggact ttgtatttca ctagggtacaa 1020
tggaatacaa cctttgacaa gattttcaga ggaaaaatac actgtttggg caagttaagg 1080
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atgtgtttat gtgttcagat tttaatagag attcaaaaat gactcatttt taccaataat 1500
gttaaattag ttttggttgt gctagcatga attaataacc accattttat accagtatca 1560
tcagtgaaga attgtatttc aagattcaaa caataaccag caattaaact tttttctaca 1620
atgtaaaaaa aaaaaa 1635

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&lt;210&gt; 126

&lt;211&gt; 2673

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 2779172CB1

&lt;400&gt; 126

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cagggggcctt tcctcagaga atatctttat gtttacaaga atgtaagtca gctgtcacca 60
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ttttggccat gacagacgac cagcggatgg tgaaaaacaa gcagctactc atgtaagtct 180
tgatcaagaa tatgattctg aatcctctca gcagtggcga gaacttgagg aacaagttgt 240
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cagttactca gataattcaa gatttccact tgcagttgta gaagaaccaa ttacagtggg 360
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agaaattcaa ggtcctcgac ttaacaacac aaaagaagag aaaacatctg ttaaataatg 780
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ggaattccac atagtgaag tatcaagtag tagcaaacac tggaagttac agaaatttgt 1500
aaatctttct gaaaacaaag ataccaaaact tgcagtagg gagaagggaa agttttgtct 1560
taaggcaata agatgtgaga aagaagaagc ggccacacag tctctgaaa aatatacctt 1620
tgcagatata atctttggaa atgaacagat aataagttca gcaagcccat gtgcagactt 1680
cttttatcga agtttatctt ctgaattgaa aaaaccacaa gctcacttgc ctgtgcatac 1740
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&lt;210&gt; 127

&lt;211&gt; 2206

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 3279329CB1

&lt;400&gt; 127

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&lt;210&gt; 128

&lt;211&gt; 1426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte clone 3340290CB1

&lt;400&gt; 128

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 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte clone 3376404CB1

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<220>  
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